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# Venereal Disease Information

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FEDERAL SECURITY AGENCY  
UNITED STATES PUBLIC HEALTH SERVICE

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# Serial Examinations in the Epidemiology of Gonococcal Infections

Samuel D. Allison, M. D.,<sup>1</sup> W. L. Zink, M. D.<sup>2</sup> and W. S. Ito, M. D.<sup>2</sup>

In May 1942, an order was issued by the military governor of Hawaii, supplementing and strengthening previously existing Board of Health regulations, which charged the health department with certain measures, among which was the investigation of contacts of venereal disease cases. All persons who contracted a venereal disease were required to disclose the name and/or other identification of the person from whom the disease might have been acquired for health department use. In order to permit earliest possible investigation, all physicians including medical officers of the Armed Forces were directed to report every case of venereal disease to the health department within 24 hours after the diagnosis had been made. The health department was to investigate each case immediately.

Following the issuance of the order it was decided to examine "suspected sources" of gonorrhea on at least 3 consecutive days, with further examinations being made if equivocal results were obtained. In this study, for the most part "suspected sources" were contacts of cases of gonorrhea reported by the armed services or persons referred for examination by the civil or military police. Serial examinations were considered necessary as most of the women examined were professional or clandestine prostitutes in whom infection is often difficult to detect.

The first examination consisted of cervical and urethral spreads and cultures, and subsequent ones, of cultures only (1). Spreads were stained by the Gram technic. Exudates for culture were collected on sterile swabs moistened with nutrient broth, placed in a tube containing 0.15 cc. of broth, and sent to the laboratory for cultural diagnosis after the manner described by Carpenter (2). Transportation of the specimens caused an unavoidable delay of from 1 to 3 hours between taking the specimen and planting the cultures.

As all of the women examined were either contacts of cases of gonorrhea or were known to be promiscuous, the presence of typical gram-negative intracellular diplococci in the spreads or typical oxidase positive colonies of gram-negative diplococci on the culture medium was considered sufficient evidence for the diagnosis of gonorrhea. If positive spreads were found at the time of the initial examination the individuals were placed under treatment and no attempt was made to verify the diagnosis by cultures.

In order to determine whether the examinations should be made on 3 successive days or the number reduced, a study was made of the effectiveness of the first as compared with subsequent examinations. The series here reported consists of 80 cases, all of which would have been given at least 3 examinations had not infection been discovered earlier in the series. Of these, 47 (59 percent) were found infected on the first, and 33 (41 percent) on subsequent examinations.

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*Individuals found infected through examination of "suspected sources"*

First examination positive		Second examination positive; previous examination negative		Third examination positive; previous examinations negative		Subsequent examination positive; third examination doubtful		Total
Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number
47	59	16	20	15	19	2	2	80

Known infected promiscuous women were placed under surveillance by the health department. Prior to their release from surveillance but following "cure" and repeated examinations by private physicians, clinics, or the Army Provisional Hospital in which many of the patients were hospitalized, these women were then reexamined serially by

the health department using the previously mentioned method.

Thirty individuals were found to have evidence of gonococcal infection at the Health Department Clinic following treatment and examination by the above mentioned agencies. Of these only 14 (47 percent) were found positive on the first, and 16 (53 percent) on subsequent examinations.

*Individuals found infected following treatment and examination by private or public treating agencies*

First examination positive		Second examination positive; previous examination negative		Third examination positive; previous examinations negative		Subsequent examination positive; third examination doubtful		Total Positive
Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number
14	47	9	30	5	17	2	6	30

#### SUMMARY AND CONCLUSION

1. The effectiveness of single as compared with serial examinations for gonorrhea was studied in a group comprised mainly of prostitutes.

2. Nearly one-half of the contacts and treatment rechecks found infected would have been missed had serial examinations not been performed.

3. Multiple examinations seem essential for the discovery of gonococcal in-

fections among contacts of this type and among treated patients being examined prior to release from surveillance.

#### REFERENCES

- (1) Laboratory work performed at the Board of Health Laboratory.
- (2) CARPENTER, C. M.: The gonococcus (*Neisseria gonorrhoeae*). Diagnostic Procedures and Reagents, New York, American Public Health Association, 1941, pp. 85-111.



# Venereal Disease and Selective Service

Richard H. Eanes, Colonel, Medical Corps, U. S. Army

Despite advancements in science which seem at times almost unbelievable, the old, old problem of venereal disease is still with us. Through the ages this problem has been ever present. In times of mobilization of armies, it becomes increasingly important. There is no part of this problem that is not subject to solution. We have faith that our age has accomplished much toward eradication, but the mere existence of these diseases among our people is an indictment of our civilization. We have the knowledge, we have the means; we should have the intelligence for at least as much control of venereal diseases as we have had of typhus fever. We have no legitimate excuse for the continuation of this state of affairs. Our people have hidden the problem from themselves; they have denied to themselves its very existence. Disagreeable subjects cannot be so disposed of satisfactorily. We should take courage; Doctor Parran, in these past few years, has done much to bring the problem out into the open, and syphilis and gonorrhea now are words that can be spoken unaccompanied by a blush or an apology.

For several reasons, "Venereal Diseases and Selective Service" will be discussed rather than "Rehabilitation of Selectees With Syphilis and Gonorrhea," as was first assigned. At the time the subject of this talk was chosen, the pilot tests of rehabilitation which were being carried out in Maryland and Virginia, but which are now closed, revealed a few cases of gonorrhea, but not enough to be of interest. The Selective Service had

given serious thought to rehabilitation of men who had syphilis. An ample program for the control and treatment of syphilis was being conducted by various States, with the support of the United States Public Health Service. Competition with this program was not desired, nor was it deemed practical for Selective Service, without police power, to undertake the treatment of syphilis over the necessarily extended period of time. All thoughts of any rehabilitation by Selective Service are at present in recess, for Selective Service is well occupied with the greater task of selecting those who are fit to serve.

In the fall of 1940, when the Selective Service System was to begin operation, it was recognized that an excellent opportunity would be offered to secure a survey of the amount of venereal diseases among men in the age groups that were to be called to service. Accordingly, by conference between the representatives of the Selective Service System and the United States Public Health Service, an agreement was reached whereby the local examining physicians of the Selective Service System would secure a specimen of blood from each registrant examined, and a second specimen when the first was not negative for syphilis. The blood tests were to be made in State and other laboratories without expense to the Selective Service System. In some States the local boards have shown much zeal in carrying out Selective Service directives on securing blood. In instances they have taxed the facilities of the State health departments and the Post Office Department. Problems necessarily arising from this crowding have been promptly adjusted by the United States Public

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Given at the Conference on Venereal Disease Control Needs in Wartime, October 21-24, 1942, Hot Springs, Ark.

Health Service. Also, each registrant was examined for all venereal diseases and any such diseases found were to be reported by the local examining physician to the appropriate health authorities, as directed by law in the various States.

The interest of the Selective Service System in this program was very real. The system was charged by the Congress with an evaluation of the manpower for the best accomplishment of a great national effort. Anything that might interfere with a registrant's ability to serve represented a very real interest to Selective Service. Apart from this official interest, there was hardly an official in National Headquarters not vitally interested in the problem per se, and how it affected not only manpower but our social system. There are sections of the country where venereal diseases affect the general manpower situation very little. However, when registrants in other areas manifest 30 percent positive serologic findings, there is indeed a tremendous withdrawal from the manpower pool.

At the time the Selective Service began to function, the Army did not require blood tests for syphilis in recruits but when men who were known to have a venereal disease were presented for recruitment, they were not accepted. As soon as it was realized that the Selective Service System, in conjunction with the State health departments and the United States Public Health Service, would make these serologic tests, the Army became much interested in syphilis among inductees. It was a peacetime procurement and the criteria for cure and acceptance by the Army were made high. At that time the Army was trying to secure for training only the pick of manhood. The original plan called for only a year's intensive training.

It is not difficult to understand the many obstacles attending any active or comprehensive participation of the Selective Service System in the prevention and treatment of these diseases. The interest in treatment, particularly of syphilis, was most important, for each man rejected by the Army because of

venereal disease meant that another man had to be selected. It became necessary that registrants, once having had a proved positive serologic test, be treated in accordance with the Army's criteria before they could be inducted. Thus, many of the State medical officers of Selective Service accepted as a challenge those criteria established for the acceptability of one who had had syphilis, and in cooperation with the State and United States Public Health Service officers, plunged into a campaign to meet the criteria for as many registrants as possible. They sought the support of the various State enforcement officers. Bills were offered in the legislatures of two States by State medical officers; one was passed for the enforced treatment of syphilis.

It may be of considerable interest to outline plans put into effect in two States by their Selective Service directors and medical officers, working in cooperation with the State health officials. The procedure in one of the States is to call the registrant in to his local board if a diagnosis of syphilis is made. His condition is explained to him, and he is told he must receive treatment in accordance with the laws of the State. He is given a card (the size of his Selective Service registration card) on which the registrant's name is printed and spaces provided for the dates of treatments, drug used, and the signature of the attending physician. The registrant is directed to his private physician, or if he states that he is unable to pay, he is sent to the nearest venereal disease clinic. The registrant is instructed to return to his local board at the end of 30 days. Upon his return, if his record card shows that he has received three or more treatments during the month, he is complimented and instructed to return again at the end of the next month.

If at the end of a month the registrant's card indicates that he has received less than three treatments, with no adequate excuse for neglect of treatment, or if he fails to return when his name is up, the county health officer is notified. If, after investigating, the health officer finds the registrant culpable, a warrant



is sworn out and delivered to the sheriff. The sheriff has to make return on the warrant, and the registrant cannot be released from custody except on order of the county health officer. Special funds were set up for this purpose, the sheriff receiving \$3 for his service.

When this program was first started there were many delinquents, but they became fewer as it became known that the law was invoked. When a registrant is released from custody by the county health officer, he is ordered to return to his local board, and the local board is notified. Delinquent cases are managed in this way until dismissed from the clinic as having received adequate treatment. Registrants who have moved from one local board area to another are checked by the transfer of their venereal disease history. Not all of the discovered cases have been treated as a result of this system; there are always some who are successful in evading any system. However, it is known that the numbers treated have ranged into the thousands.

For the successful enforcement of such a system it is necessary to have the enforcement of a good basic law, and at the same time, the cooperation of energetic, understanding law enforcement agencies. Fortunately all of these were available in this particular State, the enforcement agencies being headed by the Governor.

In the other State referred to, the State health department and Selective Service System have been working cooperatively to compel as many registrants as possible to seek treatment by advising them through the local board. They have developed a form letter for this purpose which is satisfactory.

In July 1942, Selective Service in this State adopted a more forceful and direct program. They mailed a questionnaire to 4,700 registrants known to have had syphilis. On this questionnaire, the registrant was asked to state if he knew he had syphilis before he was notified of the result of the Selective Service examination, and if so, how much treatment he had taken, both before and after his Selective Service examination. The name and address of the physician who

administered treatment was also required. Of the 4,700 questionnaires mailed, 3,185 were returned within two weeks, and of these, a total of 1,658 reported that they were under treatment.

Six hundred and eighty-two registrants admitted that they were not under treatment. The State health department sent a letter to these 682 registrants, stating that the Selective Service System had reported them as having syphilis, and as not being under treatment. This letter also called their attention to the law which required treatment. It carried an attached coupon which was to be completed and returned by the physician with whom the registrant arranged for treatment. To those who resided in a county where there was not a venereal disease clinic, the same letter was sent, with the exception that it was a little more detailed in explanation, and the doctor was given an opportunity on the return slip to state whether or not the registrant was able to pay for treatment. From the 682 letters, replies were promptly returned by 147 that arrangements for treatment had been made. A letter was sent to those physicians who had indicated that the registrant was unable to pay for treatment; payment at \$1 per treatment was authorized, and full explanations as to treatment outlined.

Many questionnaires were returned for lack of proper address; these are being traced. Those registrants who failed to return the State health department's letter are being referred to the local health officer for investigation and prosecution. The law of this State requires treatment of infected people.

Further data obtained from this questionnaire revealed that 4 registrants were dead, cause unknown; 69 were actually in the Armed Forces, manner of enlistment not known, and 181 registrants had moved from the State. Those registrants who went into the Armed Forces and those who have moved from the State have been followed by notification to the Armed Forces or to the respective State health departments of the former diagnosis.

As a result of this work, it is estimated, conservatively, that 60 percent of registrants in this State who have had syphilis are under treatment. The other 40 percent are being sought and a proportion of them will be put under treatment. I think this percentage represents excellent results, but the United States Public Health Service officer who has worked on this problem has informed me that he is not content with this 60 percent; neither are we. Letters from members of the families of some of these registrants indicate that some of the men are purposely refusing treatment, hoping to avoid induction. Some have been prosecuted and imprisoned.

In this same State, the health department has observed that the number of women and children who are now having blood examinations by the various county health units has more than doubled during the last 2 years. The compulsory requirement of Selective Service for men to have blood tests has evidently stimulated voluntary testing among other citizens, thus extending the recognition and treatment of additional cases of syphilis.

The systems of these two States are perhaps the most effective which have been developed in any State, but other States have their laws and their own methods, and many of them have accomplished results which compare favorably.

Gonorrhea does not elicit as much interest as syphilis; yet it too has been a problem. It represents for Selective Service a "quick trick," so to speak. In other words, its treatment, particularly its modern treatment with the sulfonamide drugs, ordinarily produces a cure within a reasonable period of time. In gonorrhea we have found a more fertile field for Selective Service than in the field of syphilis. Selective Service has cooperated in every way possible in reporting to State health departments, and in following up those men who have been so reported. Our Boards are instructed to check and recheck all registrants rejected because of gonorrhea. As soon as they are found to be free of the disease, they are presented for induction. In

several places there has been evidence of reinfection after the original cure. The second infection may, perhaps, have been deliberately acquired after the registrant gained the knowledge by his original rejection that gonorrhea forestalled induction.

After the declaration of war in December 1941, it became apparent that the Army would have to accept inductees who had noncomplicated venereal diseases. Accordingly, representation was made to the War Department that arrangements should be made for the acceptance of such cases. In March 1942, the revised MR 1-9 was published; it stated that uncomplicated gonorrhea would be accepted as soon as housing facilities could be arranged for proper care and treatment. However, the same exacting criteria for "cure" as had been maintained through peacetime were required for those with syphilis.

The War Department set about arranging for the necessary facilities for care and treatment. These have not yet (October 1942) been completed, but we are assured that the time is fast approaching when they will be ready. From then on all registrants presented by Selective Service who do not have complicated venereal disease will be accepted for induction. We interpret this to mean that those with simple, acute, or chronic gonorrhea without involvement of the deeper organs, and those with syphilis other than visceral, cerebrospinal, or cardiovascular, will be accepted. This will unquestionably increase the available manpower by a considerable number.

We were informed that beginning with the present month (October 1942) 2 percent of all men inducted per day and per race might be accepted while suffering from uncomplicated gonorrhea. Very recently that 2 percent has been changed to 4 percent.

Of course we have heard from the beginning that certain registrants knowing that venereal disease would prevent their induction have deliberately contracted one or more diseases to avoid service. We have heard that there were prostitutes guaranteeing an infection for cer-



tain fees. Some of this information has come to us from authoritative sources, and there is no doubt that some venereal diseases have been contracted for this purpose. It is not believed, however, that the preponderance of these diseases among registrants was so purposely arranged. We are still of the opinion that the large majority of the cases which were new when discovered about the time for induction have been the result of carelessness or the reckless attitude brought about by the disturbance of the emotions of the registrants and their female friends.

Again considering prevention: Selective Service has been requested by the United States Public Health Service to participate more actively in a program for the prevention of venereal disease. These requests, although they have not been granted, have nevertheless always fallen on sympathetic ears. Other considerations believed to be of paramount importance have blocked their adoption. As an example, Selective Service considered sending, in the envelope with the "Order for Induction," a pamphlet on venereal diseases, which would warn the registrant of the dangers from these diseases, and give him insight into the importance of their prevention. We found that the request from the United States Public Health Service was only one of many which came from the various Government agencies, suggesting that various types of literature be sent to registrants by Selective Service. If one of these requests were granted, there could be little excuse for refusing to grant the others. If all were granted, the registrant would receive such a large number of papers that it was doubted if he could find his "Order for Induction" among them. If he did find it, its significance would perhaps be lost in the perusal of this avalanche of literature.

A total of 284,000 cases of syphilis have been found as the result of the examinations thus far performed on registrants of the first, second, and third registrations. Of these, 93,000 were among white, and 191,000 among Negro regis-

trants. Of a total of 71,000 cases of gonorrhea, 34,000 were among white, and 37,000 among Negro registrants.

These figures do not represent the number of registrants rejected because of venereal diseases. In a number of these men, other conditions were discovered which would have caused the registrant's rejection even if he had not had a venereal disease. Syphilis was found as a primary cause for rejection in 120,000 registrants, of whom 25,000 were white, and 95,000 were Negro. Gonorrhea was found as a primary cause for rejection in 30,000 registrants, of whom 14,500 were white and 15,500 were Negro. In examining these figures, it should be kept in mind that the ratio of the Negro population to the white is 10.6 to 89.4.

Basing our opinion on the experience in some States, we believe that a large number of the 30,000 registrants who were rejected because of gonorrhea have since been inducted as cured. The acceptance of men with uncomplicated gonorrhea will not mean that the Army will secure immediately 30,000 such cases. There is no way to estimate just how many cases will be presented at the time the Army begins taking such registrants. We have learned that already in some of the communities the induction stations are not having even the allowed 4 percent per day of registrants who have gonorrhea.

In spite of the earnest effort on the part of various State Selective Service officials, it is not believed that a large number of registrants with syphilis have ever been inducted. It is believed that a large percentage of the 120,000 who were found with syphilis as the primary cause of their rejection will become immediately available for presentation to the Army.

It is interesting to note the interest which has been shown by a number of the local Selective Service Board clerks. In a recent conference with four such clerks, one was especially well informed on the needs. He stated that personally he had been successful in following through not less than seven registrants



until he had them inducted. I do not know his methods. He perhaps bulldozed them or persuaded them in some way, but he succeeded in getting seven men inducted over the high criteria of the Army.

The Surgeon General of the Army, in Circular Letter No. 74, dated July 25, 1942, published a revised treatment for syphilis which it is believed represents the necessary amount of treatment to safeguard soldiers with syphilis. We are confident that a large percentage of registrants have received the equivalent of the treatment prescribed in that circular letter. When presented for induction by Selective Service they will require only a classification of their syphilis status and will not need any additional treatment for it. Of course the fact that they have had syphilis should never be forgotten. They should be continuously watched while in the service for complications not demonstrable at the time of their induction. The greater percentage of these men will do duty equivalent to that which may be performed by those who have not been so unfortunate as to have been infected with syphilis. Apart from the duty in which these men will participate, there is another problem ever before us. Can the Nation afford to take

from its males the cream of its manhood and send them forward to battle, while the diseased and less favored are left at home? We do not have to look far back into history to see a people at war, with the leaders of its manhood in the front ranks from the very beginning, because of voluntary enthusiasm, while the less favored and more reactionary elements hung back until conscription forced them. Nor are the results hard to foresee; no modern nation can afford so devastating a system. In war all must serve who are physically or mentally fit to render service.

I have already stated that we have the knowledge, the insight, and the means sufficient to eradicate these diseases from our civilization. It behooves us, therefore, not to try to find excuse for their existence among us. Instead, we may expend that energy better in the effort dedicated to creating a broad national program for the study of these diseases, for their detection in the individual, and for their treatment and cure, until they are brought under control and no longer constitute a national menace. To this program, may I assure you, the Selective Service System will lend its supreme support and assist whenever and wherever such assistance is possible.

# Improvement of Present Methods for Extrafamilial Contact Tracing

Mary A. Burke, Consultant in Social Hygiene Nursing, Detroit Department of Health

Case finding in syphilis and gonorrhea is war work. In spite of depleted staffs, present case-finding methods must be improved because these two diseases destroy the manpower of our country. All public health nurses who are assigned to the home front must be charged with the burden of contact tracing in this field. To do this, every community should make a very careful analysis of the present public health nursing program in order that the limited available nursing service can be so distributed that its maximum value will be secured.

Throughout the years, physicians, social workers, male investigators, and specialized nurses have carried on the greater part of the program of extrafamilial contact tracing in gonorrhea and syphilis. Their persistent work has brought case finding in this field to its present degree of efficiency. Today, many planned programs throughout the country are being upset because many physicians who served as epidemiologists and experienced male investigators are answering the call to the Armed Forces or to war industries, and each month 3,000 American nurses are being called to military service.

Because gonorrhea and syphilis sabotage the national war effort, every public health nurse who is assigned to duty on the home front should spend a part of her time each day on gonorrhea and syphilis case finding. The public health nurse in uniform doing family work, whether she is in the field, in the clinic, or in the in-

dustrial plants, can contribute immeasurably to extrafamilial contact tracing. Tangible results will be seen in terms of a higher case-finding ratio.

Because these venereal diseases affect the health of millions of persons in the United States, the problem can never be adequately handled even by hundreds of nurses specializing in gonorrhea and syphilis work. Twenty-three thousand public health nurses, making over 29,000,000 family visits each year by devoting part of their time each day, are needed to reach these millions of persons if progress is to be made. There are many reasons why some health officers will not subscribe wholeheartedly to such a part-time plan. Some believe that it is impossible for a public health nurse to perform equally well in all branches of nursing. They compare the nursing field to the medical field. They will say, "When you need an operation, get a surgeon. When a baby is to be delivered, get an obstetrician. You don't go to a syphilologist when you have tonsillitis." We will agree that specialists are needed in the medical field because of the intricate details of diagnosis and treatment, but nurses do not have such responsibilities and, moreover, few if any diseases can be treated successfully without considering the patient's relationship with other members of the family group or the family situation. We must remember too that there is always a group problem; even if the patient is a single man or woman living in a rooming house he or she is a part of some family-type group.

The health officer who thinks in terms of the nurse specialist compares her field

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to the same field in medicine; yet they are not analogous. The physician needs to know much more about surgery, syphilology, and other specialties than the nurse needs to know to give expert nursing care in these same fields. The unlimited knowledge that a physician must have to do his work well in each field makes it easy for him to believe that the nurse specialist is more capable of carrying out the syphilis and gonorrhea program than the generalized nurse.

The desirable essentials for all public health nursing work are also needed in gonorrhea and syphilis work. These essentials include, in addition to the basic course in an accredited school of nursing, at least the content of 36 college hours in public health nursing, and practical public health experience under supervision. The public health nurse needs special training in the control of communicable diseases, in the recognition of social problems, in the study of the causes of human behavior, in health education technics, and in the basic technics of social guidance. She must possess sympathy, tact, friendliness, an ability to understand patients and their problems, a genuine interest in the program, and an ability to interpret physicians' instructions so that patients will understand them easily. These essentials are necessary to a public health nurse's success, whether she is giving nursing care for a scarlet fever or prenatal patient, or the extrafamilial contact of a gonorrheal, tuberculous, or syphilitic patient.

In order to work in the field of gonorrhea and syphilis, the public health nurse needs to have a thorough knowledge of these diseases, not the same as the physician possesses, but enough to interpret intelligently his orders. Generalized nurses cannot become proficient in the field of gonorrhea and syphilis merely through listening to lectures, attending classes, reading books written by specialists, and observing the specialist in action. To complete the nurse's experience, she must work with patients, must observe how they react to what she has said to them. Staff education programs that permit nurses to observe work which

has been well done, to participate in the work, and then to demonstrate their ability to the supervisor, will offset any notion that generalized nurses cannot serve in this field as well as they do in others.

The second objection is often stated as: "Not every nurse in the program can be trusted to do this highly important job—only the 'topnotchers' will ever be permitted to participate." It is well for us to remember that the world's work is done by average persons. Many average nurses, ever conscious of the program to control gonorrhea and syphilis, can do more work and produce better results than can a few very superior nurses. A nurse in a large clinic, who was considered as only average, "sold" more spinal fluid tests to patients in 1 month than did three other nurses who were considered to be unusually well informed. Observation disclosed that of equal importance to the information which she imparted were her sympathy and genuine interest in her patients. We need to keep in mind that "topnotchers" have no corner on sympathetic understanding, on sincere interest in the welfare of others, or on obtaining cooperation.

There may be some nurses on generalized nursing staffs whose basic training did not include syphilis and gonorrhea. A few of these nurses may not feel able emotionally to prepare themselves for this work. These nurses only should be excluded from venereal disease work. Every other general nurse who wants to participate should be permitted to do so. It is safe to assume that the nurse who is interested will get the information she needs to do the work well.

There are some physicians and nurses who believe that even the well trained nurse specialist may not participate in all phases of the program. This is frequently the attitude toward follow-up visits to single persons living at home or in a rooming house. It is often felt that these patients wish to conceal their infection and that a visit by the specialized nurse would jeopardize their secret. The public health nurse's training especially prepares her to handle such delicate situ-



ations with tact. Since she is doing generalized nursing work in the district, there could be a number of reasons for her calling at the home of these individuals.

By observing a number of calls on single persons by generalized nurses in a certain area, it was found that the nurses often carried family records on members of the household. This observation in the field also revealed that most of these single persons did not hesitate to tell members of the family about the infection. The mother, aunt, or landlady was often aware that the person attended a clinic, and in most instances knew why treatment was needed. We are inclined to believe that all patients react to situations in the same manner as we ourselves would under similar circumstances. Not all persons are ashamed and upset when they learn they have syphilis or gonorrhea. One nurse in a generalized program asked a patient, who was single and living in a rooming house, why she did not report to the tuberculosis clinic for an X-ray. She said, "I can't, nurse, I go to the social hygiene clinic on Friday for gonorrhea." This patient, who was a post-sanatorium tuberculosis case, had announced as proudly that she attended a gonorrhea clinic as she would boast of a coveted membership in a club. Because this patient was a single woman living in a rooming house, the district generalized nurse had not been routinely informed of her attendance at the social hygiene clinic.

Some physicians and nurses believe that it is not safe for nurses to follow gonorrhea and syphilis contacts who live in rooming houses, cheap hotels, and brothels. They do not, however, fear for her safety as she goes into the same houses on case-finding expeditions in tuberculosis and other communicable diseases. Public health nurses in a generalized program are expected to do all other kinds of nursing service in these same environments. A single man or woman residing in a rooming house or a cheap hotel who is a contact to a tuberculosis case is visited by the generalized

nurse. If the same man or woman is a contact in gonorrhea or syphilis, he or she is often deprived of the special service which the generalized public health nurse is prepared to give. Persons without a medical background are sometimes chosen to do this work because of their special ability to force a door or to assume the disguise of a prospective customer; by such means they often succeed in bringing the alleged contact in for examination. The persuasive methods of the generalized public health nurse will surpass application of force or any undercover methods.

With regard to her safety, the poise and the uniform of the public health nurse are sufficient protection. In the slums of a certain city where police officers patrol their beats in pairs even in daylight, public health nurses in uniform go alone in safety. The uniformed nurse is welcomed where other persons are looked upon with suspicion and often denied admission.

Each individual in the community has an equal right to the services that generalized nurses are prepared to give. A woman who "works" in "Hattie's Place" and who is listed as an extrafamilial contact of a case of gonorrhea or syphilis needs the health message that the nurse can bring. Experience has shown that she will listen to it. The prostitute's child who lives "across the tracks" needs to be protected against smallpox and diphtheria just as all other children in the community. When a generalized public health nurse is permitted to make such a call, she will do many things in addition to referring the child for the specific examination. She will discuss the importance of a chest X-ray, the value of normal nutrition, and other matters vital to good health. Also, the madam can be taught to place a different value on untruthful negative health reports.

Doctor Parran has said that there are at least three persons exposed to venereal disease infection for every one that comes for treatment. He has also said that it is usually true that two of these persons need treatment.

In the tremendous problem of case finding, generalized nurses must not only follow cases found in clinics, but they should assist also the private physician in follow-up work. Generalized nurses should, we believe, receive the reports of every case of early syphilis and gonorrhea found in their district, just as they receive the reports of cases of scarlet fever and tuberculosis. Many physicians who in the past have been able to do their own case finding now find it impossible to carry this burden and welcome the help of the generalized nurse. It is thought by some that public health nurses are not welcome in private physicians' offices. Public health nurses doing family work are greeted with cordiality by private physicians who use their services in tuberculosis, child welfare, prenatal, and other fields. The private physicians will not be less friendly to the nurses when they take on this important venereal disease case-finding work.

In one city a uniformed nurse specialist has successfully assisted physicians by participating in a case-holding program. Recently another nurse specialist has begun to do case-finding work upon requests from private physicians and hospitals. In another large city, nurses keep detailed records of every case of early syphilis in the office of a private physician or a hospital clinic. These cases are followed until a minimum of 20 doses each of an arsenical drug and bismuth have been received. The physicians willingly give this information to the nurses. They also ask them to make home calls on delinquent cases. In the same city physicians make appointments for the nurses to interview early cases of syphilis in their offices in an effort to have more contacts examined. These specialized nurses give evidence of successful work, readily acknowledged by their medical associates. We believe that generalized nurses with proper preparation and supervision can become equally efficient. Physicians throughout the country who are concerned with the welfare of the people of the community will be glad to have

the help of uniformed generalized nurses. In return, they will give her the loyalty and cooperation which she has given to them. Both the physician and the nurse need this kind of cooperation in protecting community health. Physicians will discover that in this field, as in all others, the generalized public health nurses are a valuable adjunct to their service.

The success of the public health nurses in this undertaking will be in proportion to the preparation given to them. To initiate such a plan successfully, small areas at a time could be taken into the program. Here generalized nurses should be given the responsibility for all the case-finding and case-holding work. The emphasis should be placed almost entirely on gonorrhea and early syphilis. A review of recent literature reveals that many health officers believe that little time should be spent during this war emergency on late syphilis, either in the clinic or in the field. The policies and routines having been prescribed by the director of the service, participants in the program should then receive uniform instruction from the nursing administrator. This will save the time of the busy health officer and his assistants. Doctor Winslow has said, "The morale of a staff is always highest when under the direction of a professional colleague."

Generalized nurses who have participated in the field work of extrafamilial contact tracing in districts in Connecticut, Georgia, Maryland and Rhode Island have reported success. A nursing administrator who supervised this work stressed the importance of an efficient nursing consultant system which sent a supervisor into the field to demonstrate each step. She believes that the time spent in introducing the nurses to the service paid high dividends later. In one State where a great part of contact tracing, both familial and extrafamilial, has been carried by public health nurses, one infected contact is found for every case of gonorrhea; the ratio in syphilis is slightly higher. This commonwealth employs public health nurses to interview infected



soldiers and sailors and follow-up extra-familial contacts.

The potential value of public health nurses in this work is affirmed by Gladys Crain, coauthor with Dr. Nels Nelson of the book, "Syphilis, Gonorrhea and the Public Health." Miss Crain's work in gonorrhea and syphilis has been an inspiration to nurses everywhere. She says, "There is every reason to believe that generalized public health nurses will rise to new heights when their services in this field are enlisted universally."

From Maine to California, from Canada to the Gulf, there are 23,000 public health nurses in clinics, in schools, and in industry. Approximately 5,000 are in wartime industry. If we enlist the efforts of each one we will not only improve extrafamilial case finding in gonorrhea and syphilis, but will also improve case holding.

Provision should be made for a continuous staff education program. Informational tests on all phases of the work should be given to the nurse entering such a service. She and the supervisor will then know on what level she must start. Review tests should be supplied at short intervals. Actual calls should be presented in conference. Demonstration should be given in the field. Some time should be devoted to an exchange of experience and ideas. The value of using different agencies and individuals in her district to assist in her work should be pointed out. Even the druggist is important. When he knows that the generalized nurse is participating in this program, there is reason to believe that he will refer patients to her with symptoms of gonorrhea and syphilis, just as he now sends the mother with a sick baby.

The clerical system should provide facilities for obtaining information for field nurses and for clinics and private physicians without loss of time. Case records should be filed in family units so that decisions made in the clinic with regard to a patient will be made in relationship to the family unit. This is

especially true when the clinic is planning a program of treatment for mothers and their children. This is not difficult in the small clinics but where the case load is large it presents a big problem. It has been found difficult to convert large individual numbering systems to family systems under the present methods of central tabulation.

Nurses should be urged to keep records of their achievements in gonorrhea and syphilis as fully as they do in their other activities. In this way they will be stimulated by their own results and the collective efforts of the group.

A huge fire of infection is raging in all parts of our country. This blaze, constantly fed as the gonococcus and the spirochete fall on fresh fields, cannot be extinguished by sporadic efforts in case finding. Thousands of persons are needed to subdue the conflagration.

Every public health nurse in this country should participate in the control of gonorrhea and syphilis. There are thousands of nurses in the war plants who could do effective work in the field of extrafamilial contact finding if they were under centralized direction. Their service would be of enormous advantage in these days when the private physician has scant time even to give needed treatment. The nurse could instruct the patient in matters regarding his infection and secure information about his contacts. This could be done when the infected industrial worker reports to her concerning his treatment. Instead, we find upon inquiry that many industrial nurses are merely doing clerical work in gonorrhea and syphilis. One nurse in a large plant in a great industrial center said the only way she was permitted to participate was to record antisyphilitic treatments.

Where generalized public health nurses have been permitted to participate, they have been successful. Every patient who sits before them is considered in relationship with other members of the family group. It must always be remembered that every person is a part of some family group.



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## DIAGNOSIS

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### **The chick embryo antigen (lygranum) test for lymphogranuloma venereum:**

**A clinical investigation.** E. B. Heisel and George Stroud. *Arch. Dermat. & Syph.*, Chicago, 48: 379-383, Oct. 1943.

The authors report the results of tests with lygranum and lygranum control on 379 patients (39 with and 340 without clinically lymphogranuloma venereum). On 209 of these cases, concurrent tests were made with human bubo pus antigen and lygranum antigen and a comparison of the results made. Of the patients tested, 82 percent showed no reaction to lygranum control. There was 93.8 percent complete agreement between results obtained from lygranum and from bubo pus antigens in the 209 patients tested.

Three (0.8 percent) of the 379 patients with clinical lymphogranuloma venereum gave negative reactions to lygranum. For 32 patients (8 percent) who gave positive reactions to lygranum, the diagnosis of lymphogranuloma venereum could not be definitely made. Seven of these 32 cases gave a history of buboes, which suggested that false positive reactions may be due to subclinical lymphogranuloma venereum.

The authors conclude that a papule 7 mm. in diameter should be considered the minimum size of a positive reaction to chick embryo antigen (lygranum). Lygranum provides a fairly reliable test for lymphogranuloma venereum, although positive reactions do not always indicate the presence of the disease.

**Yaws, cutaneous leishmaniasis and pinta.** Howard Fox. *J. A. M. A.*, Chicago, 123: 459-462, Oct. 23, 1943.

Since yaws and pinta are diseases that are due to lack of personal hygiene and are not usually acquired through insect vectors, few members of the Armed Forces will be liable to contract them. However, the medical officers in certain tropical regions will doubtless be called upon to treat many cases in the native

populations. These diseases are confined almost exclusively to the tropics. In British and American colonies the term "yaws" is used and in the French speaking colonies, "pian."

While yaws resembles syphilis in some respects, there are enough differences for it to be regarded as a separate disease. The infection is almost invariably extragenital. It is probably most often acquired through personal contact although there is evidence that it may also be transmitted by flies. Although it occurs most often in childhood, it is never congenital and does not produce stigmas as are seen in congenital syphilis. There is also a complete absence of lesions of the mucous membranes in the early (secondary) stage of yaws.

The cutaneous manifestations of secondary yaws show some striking differences from those of syphilis. An eruption on the soles, and at times on the palms, is peculiar to yaws. In yaws there is a complete absence of iritis or iridocyclitis. The late destructive or tertiary manifestations of yaws are clinically indistinguishable from those of syphilis. There is infrequent involvement of the central nervous and cardiovascular systems in yaws, and abnormalities in the spinal fluid are not present.

The clinical diagnosis of yaws is usually easy in the secondary stage, though in the late stage it is difficult or impossible. Serologic reactions are of no value in differential diagnosis, as syphilis and yaws respond similarly. Yaws responds well to arsphenamines and to bismuth compounds; mercury does not act satisfactorily in the secondary stage, which fact is sometimes considered as diagnostic.

Gangosa, goundou and juxta-articular nodes are sequelae of yaws.

Mexico and Colombia show the greatest incidence of pinta. This disease is also caused by a spirochete morphologically identical with the organisms causing yaws and syphilis. Its manifestations are pigmentary changes in the skin, and these often become very disfiguring in the dark skinned people in whom the disease occurs. The early lesions respond

well to antisyphilitic treatment and it is not a serious disease except for the cosmetic defects.

**Serological tests for syphilis in large H. M. ships under war conditions.**

R. P. Crick. J. Roy. Nav. M. Serv., London, 29: 196-197, July 1943.

The author feels that the value of serologic precipitation tests for syphilis in large ships in wartime overrules the objections to their use. In some cases earlier treatment can be instituted and a better follow-up procedure carried out because of them. The chief objections are: (1) The inexperience of the operator renders the test unreliable, (2) the expense of antigen and the question of its keeping qualities under diverse climatic conditions and the provision of apparatus, and (3) these tests can be carried out in hospital ships and shore establishments and are hence not only unnecessary but undesirable as a far higher standard of accuracy may be expected in such laboratories.

The author agrees that in peacetime these objections would carry much weight, but exceptions have to be made under the present conditions. To overcome these objections he recommends the use of the Meinicke clarification test (Ford Robertson-Colquhoun modification) which requires only reasonable care and intelligence. The antigens used for this test have been kept in a cupboard protected from strong light at room temperature in extremes of climate for a year without bad effects. The equipment necessary for the tests consists of a few small test tubes and three graduated 1 cc. pipets. The interpretation of the test is simple.

During the past year, of 69 tests 36 have been paralleled by the Kahn test and 4 by the Wassermann reaction in hospital ships or shore establishments. There was one disagreement and repeated tests showed the Meinicke test to be correct and the Kahn falsely negative. In this case treatment was delayed because of the falsely negative Kahn test. The use of the Meinicke test on large ships has proved of value in darkfield-negative

sores and suspicious rashes. It can relieve the hospital ships in routine blood examinations during continuous treatment and is useful as a test of cure.

The uncontrolled use of this reaction under poor conditions is not advocated to the exclusion of hospital laboratory tests, but it is recommended merely as an adjunct in certain circumstances. The author feels, however, that this simple precipitation test has a definite use and is justifiable in large ships under war conditions.

**Juvenile paresis, diagnosis and prognosis: A report of eight cases.** Louis A. Lurie, J. Victor Greenebaum and Sol Levy. Urol. & Cutan. Rev., St. Louis, 47: 571-575, Oct. 1943.

Among the 1,850 children studied in 20 years at the Child Guidance Home, 2.5 percent were syphilitic, and of these 32 showed involvement of the central nervous system. The 8 cases in which it was possible to make a diagnosis of juvenile paresis were followed from 6 to 20 years. There were 5 boys and 3 girls in the group, with ages ranging from 6 to 12 years at referral. In all but 1 case there was a positive history of syphilis in one or more members of the family; in 4 cases there was a history of neurosyphilis in the parents. Only 2 of the children were feeble-minded at the time they were first studied, but they all showed a characteristic steady and progressive mental and intellectual deterioration. There was intellectual regression to a state of simple dementia with confusion and inadequate emotional responses, motor restlessness, untidiness, destructiveness, and antisocial activity.

In 7 of the cases the blood serologic reaction was positive for syphilis, and in 3 of the 6 cases in which spinal examination was done, the test was positive.

Six of the children received antisyphilitic treatment for varying lengths of time following their discharge from the Home. Malarial or heat treatment was recommended, but only 2 received either therapy. Two of the treated chil-



dren died, one 6 years and one 3 years after diagnosis had been made. At the present time, none of the children have been able to make satisfactory social or industrial adjustments.

**Nephrosis associated with early active syphilis.** Arthur Klein and William B. Porter. South. M. J., Birmingham, 36: 694-697, Oct. 1943.

The patient was a Negro female 16 years of age. She was admitted to the Medical College of Virginia Hospital, complaining of swelling of her face of 4 days' duration. A diagnosis of nephrosis and gonorrheal involvement of the lower genital tract was made. There was no improvement in her condition after 3 days' treatment with a high-protein, salt-free diet and limitation of fluid intake, and a typical secondary syphilitic eruption appeared. Her blood serologic reactions were positive for syphilis. An initial injection of 0.04 gm. mapharsen was given and immediately the urine output rose sharply, the clinical edema disappeared, and her weight fell from 103 to 89 pounds. Mapharsen and bismuth injections were continued for 3 weeks and she was discharged from the hospital, to return for further anti-syphilitic treatments. This she failed to do, but when she was seen 7 months later, examination revealed no abnormalities of kidney function. Her Wassermann reaction was still positive and anti-syphilitic therapy was continued.

Among the infections which apparently may cause the nephrotic syndrome, syphilis is one of the most definite. Spirochetes have been observed in the urine in the absence of any evidence of nephritis, but in many cases of syphilitic nephrosis no treponemas are discovered. No spirochetes were found in this patient's urine. Results of treatment with arsenicals were remarkable in that albumin disappeared from the urine within 48 hours with concomitant diuresis and loss of edema. Although the total and fractional serum proteins were normal at the time of the patient's discharge, the cholesterol level was still

elevated, but it was normal 7 months later.

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## TREATMENT

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**Acute visual impairment during tryparsamide therapy.** Wm. B. Potter. South. M. J., Birmingham, 36: 697-701, Oct. 1943.

Of approximately 500 patients receiving tryparsamide therapy for tabes or taboparesis, 4 showed acute visual reactions. Past history or physical examination showed no disease which might be considered as contributing to the visual complications. All cases received a standard dose of 3 gm. tryparsamide intravenously, and in each case the visual reactions occurred 24 hours after the first or second injection. In 2 patients contraction of the visual field to within 5 degrees of the fixation point was noted; in the other 2, central and peripheral vision were completely lost. Two patients were followed for a period of 1 year; one showed approximate return of vision to normal, the other little improvement. With the appearance of this reaction, the anti-syphilitic treatment was discontinued, fluid intake increased, large doses of thiamin hydrochloride given, and spinal fluid drainage accomplished in 1 case.

The author's conclusions are that there is little etiologic similarity between the acute and the chronic types of visual deterioration due to tryparsamide. The acute reaction occurs in somewhat less than 1 percent of persons receiving tryparsamide therapy; usually it occurs after the first or second injection, and bears no relation to the amount of drug injected, the age or sex of the patient, or other detectable systemic or ocular factors. Prognosis must be considered to be only fair in this type of reaction, although the evaluation of the various means of therapy in such cases is incomplete.

These 4 cases are described in detail.



**Resistant syphilis (nonresistant in wife).** H. J. Templeton. *Arch. Dermat. & Syph.*, Chicago, 48: 412-413, Oct. 1943.

The author reports a case of a man with syphilis resistant to treatment, while his wife's infection, apparently contracted from him, followed a mild course. The patient was a 30-year-old white man with extensive mucous patches in his mouth and a widespread papular secondary eruption. He had had a penile lesion 3 months previously. The blood Wassermann reaction was strongly positive. The lesions on the skin and in the mouth persisted after 8 weekly injections of mapharsen and a bismuth preparation. The use of arsphenamine, and later the bismuth preparation together with an injection of typhoid-paratyphoid vaccine, brought no improvement. Intensive treatment, consisting of 0.06 gm. mapharsen twice daily for 8 days and 2 sessions of artificial fever up to 106° F., produced by the hypertherm, caused the lesions to disappear within a month. The bismuth preparation was continued twice a week. The patient remained under treatment, but his Wassermann reaction remained strongly positive.

At the time the patient was first seen his wife also was examined. Her Wassermann reaction was negative. Two months later it was found to be strongly positive and she had a faint maculopapular, clinically typical syphiloderm. Mapharsen 0.06 gm. was given twice weekly for 16 injections. The lesions disappeared rapidly within the first 2 weeks. Her Wasserman reaction remained positive.

The author concludes that some unknown factor in the individual rather than the drug or the variable virulence of the spirochete determined the course of the disease in these cases.

**The use of acetylarsan in the treatment of congenital syphilis in children.** Joseph Yampolsky and Charles C. Powel. *J. Pediat.*, St. Louis, 23: 303-306, Sept. 1943.

Acetylarsan is a pentavalent compound containing 21.5 percent arsenic. It oc-

curs as a white powder freely soluble in water, and is usually administered by subcutaneous or intramuscular injections, although it may be given intravenously. The dosage given intramuscularly is 0.5 cc. (0.025 gm.) for 20 pounds of body weight. In the course used by the authors no rest periods were given and the patients usually received from 20 to 40 weekly treatments continuously. The drug seems to be well tolerated by children; no vasomotor reactions were noticed, and no delayed reactions giving rise to late jaundice or exfoliative dermatitis.

The patients the authors have treated by means of acetylarsan are divided into two groups. Group 1 was comprised of 11 patients between 3 weeks and 1 year of age. All skin lesions cleared up very promptly, although most of the patients received 20 to 30 injections. Four of the 11 patients had serologic reversal; the remainder continued to have a positive Kahn test after 20 to 30 treatments. In 6 infants in whom syphilis was demonstrable by roentgenograms before treatment, 3 showed marked improvement and 2 showed no evidence of syphilis.

Group 2 consisted of patients from 1 to 12 years of age. Their secondary lesions remained unimproved except in 1 case. This patient had iridocyclitis, which healed after a few treatments. Serologically the condition of the patients remained positive before and after treatment. The 1 case which had roentgenographic indications of congenital syphilis remained positive after 36 treatments.

These findings indicate that the drug must be used for a long time in order to bring about serologic reversal in the very young. Older children do not respond to the drug alone.

**Artificially induced fever as a therapeutic procedure.** William B. Carson. *Psychiatric Quart.*, Utica, 17: 604-616, Oct. 1943.

A series of 139 patients, 122 with general paresis and 17 with cerebral syphilis, was observed at the St. Lawrence State Hospital. All patients had positive

spinal fluid and about 5 percent had negative blood Wassermann reactions. The inductotherm was used to induce fever.

The 122 general paretics received a minimum of 70 hours of fever, with at least 30 hours at or over 106° F. Many received more than 70 hours. Treatment was not stopped while the patient showed improvement. Sixty-seven percent of the group showed improvement; 15 percent died. The estimated remission rate was 46.5 percent. Of the 17 cerebral syphilitic cases, 76 percent showed some improvement; 12 percent died; a remission rate of 53 percent was noted. All except 37 of the patients in the series received tryparsamide; of these, 27 are out of the hospital, 5 are in the hospital and 5 are dead.

In addition, 5 patients with tabes dorsalis with gastric crises received chemotherapy as well as fever therapy, usually in the form of mapharsen and bismuth, although 2 had tryparsamide. Three also received thiamin chloride. All were improved. Three cases of juvenile paresis were treated with fever therapy and tryparsamide; one was improved and left the hospital, one showed improvement but remained in the hospital, and the other was unimproved. Twelve patients with sulfanilamide-resistant acute gonorrhea were treated, with recovery in 10. Six patients with pulmonary tuberculosis and general paresis were treated, with no ill effect.

Patients with a decompensated heart should not be treated. Of the 139 patients, 24 had heart disease.

Some cases of general paresis with a history of convulsive seizures were treated successfully by giving phenobarbital before and during the artificial fever treatment. Two deaths occurred which were definitely associated with treatment, giving a mortality rate of 1.6 percent.

The author has had no opportunity to study the use of fever therapy as a prophylactic against the development of general paresis in syphilitics but he feels that the idea has merit and further work should be done in this field.

**Serum sickness and analogous reactions from certain drugs particularly the sulfonamides.** Warfield T. Longcope. *Medicine*, Baltimore, 22: 251-286, Sept. 1943.

The author feels that the problem of serum disease should be considered, especially since the toxic reactions following the therapeutic use of a number of drugs, particularly the sulfonamide group, resemble in certain respects serum sickness. Of the numerous intoxications resulting from arsenotherapy, erythema of the ninth day, "Milian," resembles serum sickness most closely. Although this reaction is best explained as a sensitization phenomenon closely resembling serum disease, it has been almost impossible to obtain definite evidence of specific sensitization in these patients. The patch test to arsenicals and related compounds has rarely been found positive, and the transfer of passive sensitization by the Prausnitz-Küstner method has also been reported to be negative.

The commonest early unpleasant effects following the administration of the sulfonamides are nausea, vomiting, cyanosis, headache, dizziness, mental confusion, and acidosis. These symptoms are probably to be ascribed to an intoxication by the drug. In general the toxic reactions following the use of all of the sulfonamide drugs fall into three categories: (1) acute hemorrhagic anemia; (2) agranulocytosis; (3) febrile reactions accompanied in most instances by cutaneous eruptions. There is increasing evidence to indicate that these toxic reactions to the sulfonamides are expressions of an allergic response to the drugs.

It seems justifiable, after consideration of the entire problem, to conclude that many so-called toxic reactions following the administration of the sulfonamides, as well as some other chemical drugs, are analogous to serum disease, and are due to a sensitization to the chemical or to one of the radicals of which it is composed. These intoxications appear in the form of the normal serum sickness, the accelerated serum sickness and the immediate serum reaction. These differ



from serum disease in the particular that specific antibodies have not been demonstrated so far in the serum, and that skin reactions to the specific drug are rarely obtained.

A bibliography, comprising 106 references, is appended.

**The use of the suppository as a vehicle in sulfonamide therapy.** James H. Park, Jr. *J. Pediat.*, St. Louis, 23: 326, Sept. 1943.

The various sulfonamides are usually administered by mouth in plain or enteric-coated tablet form which is designed to prevent gastric irritation and to facilitate intestinal absorption. Unfortunately, they frequently pass unaltered through the intestinal tract.

In order to avoid the distressing symptoms of nausea and vomiting which frequently attend the giving of sulfonamides by mouth, the author has been prescribing these drugs in suppository form per rectum, especially in the treatment of infants and young children. The base employed in making the suppository is cocoa butter, which melts quickly in the rectum, leaving the drug available for reasonably rapid absorption. Any desired dosage may be utilized. However, 7.7 gr. and 15.4 gr. suppositories of the preferred sulfonamide have been found satisfactory in most instances. The rectal dose is twice that given by mouth.

A cleansing warm water enema should be given 30 minutes before beginning treatment. A parent or nurse may be instructed to insert a suppository into the rectum at stated intervals. The buttocks should be held firmly together for 15 to 20 minutes, with adhesive tape if necessary, to prevent expulsion.

The author says that gastric irritability due to oral administration of sulfonamide has been avoided entirely by the use of the suppositories. Blood level estimations have demonstrated that this method of treatment is as efficacious as that by mouth.

**The local use of sulfonamide compounds in dermatology.** Harold N. Cole. *J. A. M. A.*, Chicago, 123: 411-417, Oct. 16, 1943.

The author reviews the literature on the local use of sulfonamides.

The use of powdered sulfonamides is practically a specific for chancroidal infection. Combes and Canizares used 80 percent starch, Lepinay used the same or pure sulfanilamide powder dusted on the ulcer alone, and many other investigators have had beneficial effect not only with the internal use but also the local use of sulfonamides. The author recommends the use of these compounds for chancroidal infection. The ulcer is first cleansed, then the powder is dusted carefully on the ulcer, where it adheres and seals the ulcer. It may be soaked off and replaced daily or every other day. Usually the ulcer heals in a week. If ulceration persists, complicated with concomitant bubo formation, oral sulfonamide treatment is recommended.

Except in the treatment of chancroidal infection the use of powdered sulfonamides has been unsatisfactory because they are unevenly distributed and as a rule do not stay on the wound. They should not be used more than 5 days since there is danger of sensitizing the patient and so preventing their use at some other time for a more serious condition. The sulfonamides should be used only when other measures have failed.

**Sulfamerazine: A clinical study of its pharmacodynamics, therapeutic value and toxicity.** Paul O. Hageman, Carl G. Harford, Sidney S. Sobin and Roy E. Ahrens. *J. A. M. A.*, Chicago, 123: 325-330, Oct. 9, 1943.

The authors treated a series of 103 patients (37 meningococcic, 17 pneumococcic, 15 streptococcic, 4 urinary tract, and 30 miscellaneous infections) for a period of 4 months with sulfamerazine. All were given an initial dose of 4 gm., orally when feasible, and 1 gm. mainte-



nance dose every 8 hours thereafter. The dosage was modified up to 8 gm. initial and 2 gm. maintenance dose every 8 hours in severe cases. Blood concentrations were measured every 24 hours just preceding the 8-hour dose. Sulfamerazine concentration determinations were done by the Bratton and Marshall method. In all these cases the treatment was uniformly good.

In the 37 meningococcic infection cases, all but 5 recovered. These 5 patients were elderly with complicating hypertension, hemiplegia and kidney insufficiency. Three pregnant women in this group recovered without apparent harm to the fetus. Of the 17 pneumococcic infections, 1 with meningitis and bacteremia died. Of the 15 patients with streptococcic infections, 1 developed an abscess containing sterile thin pus but recovered. One patient with severe uncontrolled diabetes with advanced gangrene of one foot died. In the 4 patients with urinary tract infections 1 patient with cystitis and carcinoma of the prostate died. The 30 patients with miscellaneous diseases including gonococcic and staphylococcic infections gave results comparable to those observed with sulfadiazine therapy.

The toxicity of sulfamerazine has been critically evaluated. The incidence of drug fever and rashes seemed to be about the same as that observed with other sulfonamides. Crystalluria without hematuria was observed in 7 cases (6.8 percent). One patient who had received large amounts of the drug showed concretions of acetylsulfamerazine in both ureters at autopsy. Hematuria was observed in 9 cases (8.7 percent). In all but 1 or 2 instances these patients were given large doses of the drug. The occurrence of hematuria could not be related to the blood concentration of the drug. The average fluid intake for the preceding days in 2 of the 3 cases of gross hematuria was only 1,730 and 1,875 cc. respectively, which may give some indication of the results to be expected in tropical climates. Four of the 9 cases had hemorrhagic skin manifestations, which suggests similar lesions in the

kidney. In 6 of the 9 cases the hematuria was discovered only by microscopic examination, which indicates the close watch for this manifestation. Symptoms cleared promptly with cessation of therapy without any impairment of kidney function.

The chief reason for clinical trial of sulfamerazine was the possibility that it might produce fewer and less severe urinary complications than sulfadiazine in warm climates under military conditions. It was found that less of the drug is needed for comparable blood levels, but no conclusion can be drawn as to whether urinary complications occurred more or less often than would have been the case had sulfadiazine been used, although in certain of these cases circumstances under which the drug was administered offered an excellent opportunity for urinary complications. The authors state that it seems likely the accumulated results of other observers may indicate that sulfamerazine produces fewer renal complications than sulfathiazole and sulfadiazine.

**The present status of sulfonamide therapy.** Francis C. Lowell. M. Clin., North America, Philadelphia, 27: 1247-1255, Sept. 1943.

The author says that a knowledge of the accepted principles with regard to the mode of action of the sulfonamide drugs is helpful in the management of infections: (1) The sulfonamide drugs act by interfering with the metabolism of the organism. (2) This action is decreased or abolished by substances in pus and necrotic tissue. (3) Pathogenic organisms which have been retarded in their growth because of sulfonamide therapy and in consequence have become less invasive, regain their former invasiveness and disease-producing characteristics when therapy is stopped. (4) The sulfonamide drugs do not enhance natural or acquired immunity nor do they neutralize toxins. For this reason, serums are sometimes necessary in addition to chemotherapy. (5) Recovery from infection during sulfonamide ther-

apy depends upon both the action of the drug on the pathogenic organism and the natural defenses of the body. It follows that every attempt should be made to carry out general supportive measures during chemotherapy.

The nature of the infecting organism influences the choice of the drug and the intensity and duration of treatment. A table shows the choice of sulfonamide for the different organisms to be treated. In the majority of cases the drug should be given in full dosage, and by mouth whenever possible.

Effective blood concentrations of the sulfonamides are: sulfanilamide, 10-15 mg. per 100 cc.; sulfapyridine, 5-10; sulfathiazole, 4-7; sulfadiazine, 8-15.

Acute hemolytic anemia, leukopenia, agranulocytosis, and renal complications are the most serious toxic reactions.

Sulfathiazole or sulfadiazine given in gonococcal infections in a dosage of 0.5 gm. 4 times daily for 10 days is usually effective. Patients who have failed to respond to chemotherapy alone have been treated successfully with a combination of sulfonamide and fever therapy. Sulfathiazole is given in full dosage for 18 hours. At the end of this period, chemotherapy is stopped and a fever of 103° F. is induced with the hypertherm and this is maintained for 8 hours. One course of combined sulfonamide and fever therapy is sufficient.

**The effect of sulfa drugs on the excretion of vitamin C.** Harry N. Holmes. *South. Med. & Surg.*, Charlotte, 105: 393-394, Sept. 1943.

In 1938 the author studied the amount of vitamin C in 24-hour urinary excretions of a patient, seriously ill with a streptococcus viridans infection, who was given intermittently large amounts of sulfanilamide. The patient's excretion of vitamin C was found to be 2 to 3 times the normal amount (30-40 mg.). Later the patient was given 200 mg. of vitamin C daily while sulfonamide therapy was continued. Whenever sulfanilamide treatment was resumed after interruptions of

from 1 to 9 days, the excretion of vitamin C was greatly increased.

In 1943, experiments were conducted on 10 health volunteers who were given 30 grains of sulfathiazole daily for 4 days. The excretion of vitamin C increased during the 4 days of medication to 2 or 3 times the initial amounts, and then fell off more or less sharply.

Since the body level of vitamin C must be lowered by such stimulated excretion, it would seem that the loss should be made good by the daily intake of 100 mg. or more during prolonged administration of sulfonamides. Probably part of the good effects of sodium bicarbonate when given with the sulfa drugs is due to the known checking by the sodium bicarbonate of abnormally large excretion losses of vitamin C.

**Anthiomaline in clinical medicine.** Current Comment. *J. A. M. A.*, Chicago, 123: 357, Oct. 9, 1943.

An analysis of the extensive pharmacologic and experimental studies on anthiomaline has just been made by the Office of Medical Information of the Division of Medical Sciences, National Research Council.

This drug has been used most extensively in lymphogranuloma venereum, and excellent results have been seen in from 35 to 75 percent of the 250 cases recorded in the literature. Failures have been encountered in from 10 to 25 percent of the patients. The results appear promising for granuloma inguinale but experience has been too scanty to form conclusions.

The dosage proposed is 60 mg. intramuscularly, increasing the single injections to a possible maximum of 300 mg. until a total dose of between 2 and 4 gm. has been reached. Injections ordinarily are given 3 times a week, with a repetition after an interval of several weeks.

From the information available it may be concluded that anthiomaline has a considerable variety of therapeutic usefulness and a sufficiently low toxicity to warrant its further clinical trial.



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# **PATHOLOGY**

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## **Syphilitic aneurysm of celiac artery.**

Thomas C. Laipply. *Am. J. M. Sc.*, Philadelphia, 206: 453-458, Oct. 1943.

A review of the literature shows that aneurysm of the celiac artery is rare. The author reports a case in which the aneurysm was due to syphilis. It was the only instance of aneurysm of the celiac artery in 8,070 autopsies performed at the Western Reserve University Hospitals. The patient, a Negro aged 44 years, was admitted to the hospital complaining of constant epigastric pain radiating laterally along both costal margins. This pain had been intermittent in character for over 3 years. Examination showed the heart to be slightly enlarged to the left and there were systolic and diastolic apical murmurs. In the left upper abdomen there was a pulsating fixed mass about 6 cm. in diameter. Roentgenographic examination revealed an enlarged left ventricle, slight dilatation of the ascending aorta, and calcareous deposits in the abdominal mass. A tentative diagnosis was made of syphilitic aortitis, with aortic insufficiency and aneurysm of the abdominal aorta. The blood Kline exclusion test was negative. The patient was discharged from the hospital after 5 days but visited the dispensary regularly. About 4 months later he noticed increasing weakness, shortness of breath on exertion, and night sweats and chills. His ankles became swollen. He vomited clotted blood, and his stools contained bright red blood. He continued to pass blood by rectum after readmission to the hospital. Following a large hematemesis, he died on the eighteenth day after hospitalization.

Autopsy revealed a syphilitic saccular aneurysm of the celiac artery, approximately in the midline. The aneurysm had compressed and destroyed a large portion of the head of the pancreas and there was a direct communication between the main pancreatic duct and the

aneurysmal sac. The aneurysm had partially obstructed the second portion of the duodenum and common bile duct. There was also syphilitic valvulitis and slight insufficiency of the aortic valve, and a miliary gumma in the aortic arch. No spirochetes were found in the aorta or aneurysmal wall. There were gross findings of typical syphilitic arteritis.

## **Coronary embolism: Report of a case complicating syphilitic aortitis.** H. R. Pratt-Thomas. *J. South Carolina M. A.*, Greenville, 39: 225-227, Sept. 1943.

According to the author less than 50 cases of coronary embolism have been reported, and about half of these have occurred as a complication of bacterial endocarditis. All of the 5 cases (including the present one) which have been a complication of syphilitic aortitis have occurred in Negro men below the age of 40 years.

The case reported by the author occurred in a Negro, aged 32. He had been admitted to the hospital because of three bullet wounds (in forearm, buttock and thigh). At a previous admission his blood reactions had been positive for syphilis, but the author does not mention that the patient had been given antisymphilitic treatment. The patient was in definite shock when admitted to the hospital and within a few hours began to complain of abdominal pain. Within a short time it was considered necessary to perform an exploratory laparotomy, since it was possible that one of the bullets had penetrated the abdominal cavity. No evidence of this was found, however. The patient died 9 hours after the operation. At autopsy syphilitic aortitis was found. There was almost complete destruction of the media of the root of the aorta with necrosis, scarring, hyalinization and acute leukocytic exudation. There was tremendous nodular thickening of the intima; the polypoid thrombus was attached to these internal nodules. There was extensive acute necrosis of the myocardium and fresh thrombus in the auricular appendage.



The author believes that it might have been possible that the initial shock produced by the bullet wounds produced changes in the blood dynamics responsible for the rapid deposition of thrombus material on the roughened injured intima. The possibility of coronary embolism should be kept in mind for it is probable that there is a greater incidence than has been reported.

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## LABORATORY RESEARCH

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### Gastric excretion of sulfonamide drugs.

I. H. Einsel, E. Nola Nixon, Leo Gitman and J. M. Rogoff. *Gastroenterology*, Baltimore, 1: 882-891, Sept. 1943.

One of the authors (I. H. E.) made incidental clinical observations which indicated that a marked diminution or total absence of free HCl and a decided reduction in the total acidity of the gastric juice is commonly found following effective therapeutic dosage with certain sulfonamides, especially if administration of the drug is continued when nausea and vomiting have been induced. The authors have also made observations on the influence of the following drugs, which were administered intravenously to dogs previously prepared by the introduction of a permanent gastric cannula for collection of gastric juice: sulfanilamide, neoprontosil, the sodium compounds of sulfapyridine, sulfathiazole, sulfadiazine and succinyl sulfathiazole. The findings of the clinical observations were, in general, supported by the results obtained in the experiments on dogs.

Unlike the other sulfonamide drugs investigated, after intravenous administration, sulfanilamide, sodium sulfapyridine and sodium succinyl sulfathiazole reached much greater concentrations in the gastric juice than in the blood. This may have significance in the greater tendency of sulfanilamide and sulfapyridine to induce nausea and vomiting. The experiments indicated that the volume of secretion and the acidity of the

gastric juice may be depressed, especially by sulfapyridine and sulfanilamide. However, when the excretion was stimulated by the action of histamine, not only the volume but the acidity of the gastric juice was greatly augmented, and excretion of the drug into the gastric juice was correspondingly greater. In that case, also, a significant depression in volume and acidity was produced by the drug. Sulfapyridine caused much greater nausea and vomiting than the same dose of sulfadiazine. The greater capacity of sulfapyridine for causing gastric disturbances may be associated not only with its greater concentration in the gastric juice than in the blood, but also with its more prolonged presence in relatively high concentration in the gastric juice.

**The nature of the renal lesion with the sulfonamides and its prevention with urea.** Sidney S. Sobin, Lawrence M. Aronberg and Harry C. Rolnick. *Am. J. Path.*, Ann Arbor, 19: 211-219, Mar. 1943.

From previous studies the authors felt that the in vivo use of urea might enable a distinction to be drawn between the primary nephrotoxic properties of the sulfonamide drugs and mechanical irritative effects resulting from their intrarenal precipitation. Accordingly experiments were carried out on rats. Groups 1 and 2 each were given perorally (stomach tube) 1 mg. of sodium acetylsulfapyridine per gram of body weight, group 2 receiving in addition 5 mg. of urea per gram of body weight. Groups 3 and 4 were given 3 mg. of sodium acetylsulfapyridine, group 4 receiving in addition 10 mg. of urea per gram body weight. Untreated rats of the same age were used as controls. Animals were treated over periods of 7 to 14 days, some daily, others intermittently. Serial sections were made of both kidneys and a systematic examination carried out.

It was noted that animals treated with sodium acetylsulfapyridine alone frequently had hematuria which was not constant from day to day. Hematuria was not encountered in any animal receiving urea with the sulfonamide. The former animals frequently appeared ill

and took their food poorly, but this was not true for the urea group.

Foreign material was found in many kidney sections from the animals treated with the sulfonamide alone. It consisted of precipitated sulfonamide and its acetylated products, and cellular debris with calcium and iron deposition around or on this material. Calculi were not found in the kidney sections of any animal in the urea-treated groups. In the dosage used it took 9 or 10 days before calcium could be found in mass deposits.

It was felt that the calcification in the kidney and the resultant calculus formation is dependent upon local tissue damage and the secondary deposition of calcium and iron upon focal, nonviable structures. The nephrotoxic properties of acetylsulfapyridine are mechanical in nature, and result from precipitation of the drug in the renal tract. The action of urea is independent of a diuretic effect and depends upon a specific solvent effect on acetylsulfapyridine.

**Laboratory identification of sulfonamide resistant gonococcal infections.** Walter T. Goodale, R. Gordon Gould, Louis Schwab and Virginia G. Winter. J. A. M. A., Chicago, 123: 547-549, Oct. 30, 1943.

A practical rapid laboratory method for the identification of sulfonamide-resistant and sulfonamide-responsive strains of gonococci has been developed. Pure cultures of gonococci are obtained in the usual way, prior to therapy, and small inoculums are streaked on a control plate of the Mueller-Hinton medium and on a series of 3 plates of the same medium containing sulfathiazole concentrations of 0.10, 0.25 and 0.50 mg. per 100 cc. of medium, respectively. The plates are then incubated at 36° to 37° C. for 18 to 36 hours and read. Equally good growth on all plates indicates a resistant strain; good growth on the control and no growth on the sulfathiazole plates indicates a susceptible strain; good growth on the control and intermediate degrees of growth on the sulfathiazole plates indicates a partially resistant strain. The time required for the test is from 2 to 4 days.

The authors have studied 44 cases of male gonorrheal urethritis by this method, and a high degree of correlation was obtained between the clinical response to sulfonamides and the in vitro response of the strain to sulfonamides.

The advantages of the routine use of this method in the treatment of gonorrhea are summarized as: (1) It permits an accurate prognosis of the results of sulfonamide therapy, (2) prognosis of potentially successful use of sulfonamides safely permits fewer clinical check-ups, and (3) prognosis of sulfonamide failure indicates the desirability of other forms of therapy.

**Determination of sulfonamides; a modified field procedure.** John J. Engelfried. U. S. Nav. M. Bull., Washington, 41: 1439-1444, Sept. 1943.

The sulfonamides are administered on land and at sea where no laboratory facilities are available. Therefore, the use of a simplified procedure by which the presence of sulfonamides in the body fluids can easily be determined and a quantitative estimation made, without requiring the use of a colorimeter or of reagents that are not readily available, is of great value.

The author briefly summarizes such a procedure as follows: (1) The proteins are removed by precipitation with 95 percent alcohol; (2) the alcoholic filtrate is acidified with hydrochloric acid; (3) a small piece of nitrite paper is added, followed by the addition of another piece of paper containing an azo dye; (4) the resulting color is compared to a standard solution of sulfonamide similarly treated. The use of a colorimeter is not necessary.

Comparison of the standard Navy method (trichloroacetic acid) and the modified alcohol method, which the author describes in detail, was made on 81 consecutive routine blood specimens. The results are given in a table. They indicate that the nitrite paper is of value when equipment is not available for keeping a nitrite solution in refrigeration or for the preparation of a fresh solution daily. Tests have shown that the nitrite



and dye papers stored in amber bottles at room temperature for 229 days showed no deterioration of activity. However, there is no proof that these will remain stable under severe climatic conditions.

**The Mazzini slide flocculation test—sensitivity of its antigen.** Melvin Oosting and Virginia Watson. *Am. J. M. Sc., Philadelphia*, 206: 486-489, Oct. 1943.

With the Mazzini flocculation test for syphilis, as well as with other tests for syphilis, there is a minimum and maximum degree of sensitivity of its antigen according to its age. In order to determine the conditions producing the highest sensitivity, the authors performed a series of experiments in which they employed 4 types of antigen suspensions: (1) Suspensions which had stood 4 hours at room temperature; (2) suspensions which had been refrigerated 6° to 8° C. for 15 minutes; (3) suspensions which had been refrigerated for 15 minutes at 6° to 8° C. followed by 1 hour at room temperature; (4) suspensions which had stood from 27 to 28 hours at room temperature. One series was done during the winter at room temperature of approximately 73° F. and another during the summer with the temperature in the serologic laboratory ranging from 80° to 94° F.

The results of the tests are shown graphically and are discussed at length. The graphs show that in both the winter and summer series the first type, the antigen which had stood 4 hours at room temperature, gave the greatest sensitivity, and it is therefore recommended for routine use. The antigen which has stood at room temperature for 28 hours in the winter or even in summer heat up to 94° F. was found to be more sensitive for emergency use than that ripened in the refrigerator for 15 minutes.

**The quantitative complement fixation test for syphilis in malaria-treated syphilis: Effect of the diluent.** Justin R. Dorgeloh. *Am. J. Syph., Gonor. & Ven. Dis., St. Louis*, 27: 623-628, Sept. 1943.

The influence of malaria on the reactivity of the blood in syphilitic infection

is of considerable interest. Kaplan and Brightman have recently studied the serologic reactions on 26 syphilitic patients who were receiving malarial treatment. They found that the titer in the precipitation tests rose sharply after malarial inoculation and then fell, while in the complement fixation test the titer did not increase. The diluent used in this complement fixation test was nonreacting serum, while salt solution was the diluent used in the precipitation tests.

A study was therefore undertaken to determine whether the character of the diluent influences the reaction in the complement fixation test. In 8 of the 11 cases tested the complement fixation titer with serum-diluted specimens did not rise after malarial inoculation. On the other hand, when the specimens were diluted experimentally with salt solution the complement fixation titer rose and subsequently fell in a manner similar to that of the precipitation titer. A corresponding study was made with 1 of the 2 precipitation tests; the character of the diluent had no demonstrable effect upon the results obtained.

The author believes that a rise in serologic titer following the inoculation of syphilitic patients with malarial parasites is a nonspecific one. From a theoretical standpoint, he says, the dependence of the nonspecific reactions reported here on the character of the diluent suggests the operation of physical factors rather than true serologic cross-reactions due to common antigenic components. He concludes that in cases where determination of the titer in the complement fixation test necessitates dilution of the patient's serum, nonspecific fluctuations in titer due to malaria may be obviated by using normal serum rather than salt solution as a diluent.

**An improvement of the serologic Kahn reaction in the spinal fluid.** F. Rappaport and D. Rappaport. *J. Lab. & Clin. Med., St. Louis*, 28: 1355-1356, Aug. 1943.

The authors have developed a method for the serologic Kahn reaction in the spinal fluid similar to the one used for



serum. The reagents employed are: I. (a) Kahn antigen and (b) 0.9 percent NaCl solution. II. A reliable nonsyphilitic serum (Kahn negative). The antigen is thoroughly mixed with the salt solution to the given titer and left to ripen for at least 10 minutes at room temperature.

The procedure is as follows: Pour 0.1 cc. of serum (reagent II) in each of 2 small test tubes and inactivate it at 56° C. for 20 minutes, together with a little more than 1.5 cc. of saline solution. Remove tubes from water bath and cool to room temperature. Add 0.01 cc. of the ripened antigen (I) to each of the serum tubes and shake by hand or shaker for 3 minutes. Add 0.5 cc. of spinal fluid to one tube and 1.0 cc. to the other, and again shake for 3 minutes. The reaction is read in the usual way. If a precipitate has formed only in the tube containing 1.0 cc. of spinal fluid, the reaction is weakly positive; if in both tubes, it is considered strongly positive. When there is but a small quantity of the spinal fluid available, the test may be made with one tube and 0.75 cc. of spinal fluid. To make the reaction more clearly visible, it is advisable to centrifuge at a high speed for about 10 minutes.

**Physico-chemical properties of the arsphenamines in relation to distribution and retention in the tissues.** F. B. Rodman and Harold N. Wright. *J. Pharmacol. & Exper. Therap.*, Baltimore, 79: 140-163, Oct. 1943.

Evidence regarding the distribution of the arsphenamines in the body is fragmentary, being confined to analyses of those organs which can be removed in toto from the animal body. The authors have carried out experiments on mice to account for as much of the injected drug as possible at all time intervals of the whole drug samples, as well as of the separated crystalloid and colloid fractions of arsphenamine and neoarsphenamine. A total of 308 rats was used, involving around 3,400 separate tissue analyses.

The authors reached the following conclusions from their study: The colloid fraction of both arsphenamine and neoarsphenamine is the portion of these drugs which is retained for the longest period of time. It penetrates into the tissue readily, as was shown by the sharp rise in tissue arsenic in the early time period, and it also appeared to be relatively firmly held in the tissues, since it was reexcreted quite slowly into the blood stream. The arsenic which was returned by the tissues to the blood stream was in turn eliminated from the animal body only with considerable difficulty, since a considerable portion of the injected colloid fraction was found to be still present in the blood stream at the end of 30 days. The greater part of the colloid fraction was found in the blood and liver, but the skin, muscle, bone, and intestinal tract also took up important percentages of the injected colloid fraction. All the tissues examined showed retention of the colloid fraction for a longer period of time than was shown by either the whole drug or crystalloid fraction.

The crystalloid fraction showed a high degree of initial penetration of the drug into the tissues with a subsequent rapid lowering of their arsenic concentration. The excretion of the crystalloid fraction from the tissues was much faster than was the case with either the whole drug or colloid fraction. The whole drug occupied an intermediate position, but with a decided tendency to follow more closely and more prolonged retention pattern of the colloid fraction. The distinctive affinity of arsphenamine for the liver and of neoarsphenamine for the kidney was confirmed by this study.

When injected into rats in an equivalent dosage, neoarsphenamine was found to be retained by practically all tissues (except the blood and gastrointestinal tract) to a greater extent than arsphenamine, regardless of its physicochemical characteristics.

**Trypanocidal activity and arsenic content of rat blood following intravenous administration of mapharsen.** Lawrence Peters and Harold N. Wright. (Tr. Am. Soc. Pharmacol. & Exper. Therap.) Federation Proc., Baltimore, 2: 88, Mar. 16, 1943.

The relationship of the arsenic content of rat blood following the intravenous administration of maximum tolerated doses of mapharsen to the degree of trypanocidal activity of the blood was determined by comparing the trypanocidal activity in vitro of successive dilutions of blood removed from injected rats at varying time intervals against the direct in vitro trypanocidal activity of mapharsen, using the same dilution medium and trypanosome inoculum. Cultures were examined microscopically after 18 hours' incubation at 37° C. and checked by intraperitoneal inoculation into rats or mice.

The trypanocidal period showed three phases. During the first hour the arsenic content and trypanocidal activity of the blood declined parallel to one another; the trypanocidal activity of the blood was equal to that which could be expected on the basis of its arsenic content, the percentage of arsenic possessing trypanocidal activity being 100 percent after 15 minutes, and 91 percent after 1 hour. From the second to the eighth hour, the trypanocidal activity declined much more rapidly than the arsenic level, only 15 percent being trypanocidal after 4 hours and 4.5 percent after 8 hours. Between 12 and 48 hours a secondary rise in blood arsenic occurred, but the trypanocidal activity continued to decline, only 1 percent being trypanocidally active after 12 to 18 hours, 0.5 percent after 24 hours, and the blood completely losing its trypanocidal properties after 36 hours, although the arsenic concentration was 200 times the minimum concentration required for trypanocidally active arsenic.

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## **PUBLIC HEALTH ADMINISTRATION**

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### **Venereal diseases—A Navy problem.**

Leo A. Shifrin. New York State J. Med., New York, 43: 1829-1832, Oct. 1, 1943.

The author reports on findings at the Naval Construction Training Center, Norfolk, on the branch of the Navy known as the "Seabees." The recruits range from 25 to 50 years of age, they are well educated men, and most of them are specially trained. Almost 80 percent of those who are found to have venereal diseases are married and have children. Both officers and enlisted men in the Navy are charged with misconduct whenever a venereal disease is contracted, the charge appearing on the health record, attested to by the patient as having been due to his own conduct. By keeping infected men isolated and hospitalized while under treatment, with their basic pay not being allowed for such a period, full control of the cases is maintained.

The incubation period for gonorrhea has been found by the author to vary between 2 and 31 days. The only treatment used by the Navy is 1 gm. sulfathiazole given 4 times daily for 4 days, followed by 3 days of rest, and then a repetition of the same schedule. Special care is used in administering the drug since the station is not equipped to do blood level determinations for the sulfa drugs. Complications have occurred in only 1 percent of the cases treated. These have cleared up when the drug was discontinued. Sulfathiazole has been satisfactory in almost 80 percent of cases, producing a clinical cure in from 5 to 34 days. When the patient does not respond to the drug after 20 days, 2 cc. of 10 percent argyrol in-



stilled into the anterior urethra usually produces the desired cure. In the author's experience, the Negro patients seemed to respond more quickly to treatment than the white patients. Among the Negro patients none spent more than 25 days under treatment, and none developed complications. All patients were followed up for 2 or 3 weeks after discharge from the hospital, and examined regularly for recurrence. Averages of 8 per 1,000 in white men and 50 per 1,000 in Negroes were found to have gonorrhea.

The incidence of syphilis detected in the examination of recruits is low, an average of 6 per 1,000. Mapharsen is used exclusively, with bismuth as the associated heavy metal. Treatment is usually continued for 2 years.

Only about 2 percent of those having positive serologic reports knew they had syphilis. In the remaining 98 percent there were no symptoms nor evidence of the disease. A large number of these men have had healthy children and their serologic tests taken for employment in industry have been negative. The author says that such facts lead to questioning as to whether the Kahn test by itself should be used as a criterion for diagnosis.

Chancroid is not much of a problem; cure has been rapid and complete under soap and water scrubs reinforced with sulfathiazole.

Prophylaxis is taught and prophylactic packets distributed. Navy regulations require that exposures be reported the next morning. The Navy man is then given 2 doses of 1.5 gm. of sulfathiazole each, one dose being given immediately and one at noon. No gonorrhea has developed in several thousand cases that have been so treated.

In the discussion, Wishengrad said that in the Third Naval District the routine case of venereal disease is treated on an ambulatory basis; punitive measures are avoided. Among armed guard crews, where there is no medical officer, only 1 gm. of sulfathiazole is used in prophylaxis for gonorrhea, and in the last 328 cases reported no failures have occurred.

**Labor helps fight VD.** Percy Shostac. American Federationist, Washington, 50: 11-13, 31, Aug. 1943.

For many months the Division of Venereal Disease of the San Francisco Health Department has been working with executives of the State Federation of Labor. As a result, the Executive Board of the California State Federation of Labor has recommended compulsory blood tests for all future members of the union in California. The board will inform each union concerning the free blood test services available through local health departments and will secure the cooperation of public health facilities and the California Social Hygiene Association in conducting a thorough educational program among the entire union membership.

A report to Congress by the United States Public Health Service in June 1943, disclosed that of 3,200,000 people in the United States with syphilis, approximately 1,000,000 were industrial workers.

The author points out the support organized labor can give in the fight against venereal diseases. In brief, every union should inaugurate a vigorous campaign to educate its members on the venereal diseases; they can establish social hygiene instruction in schools, aid law enforcement, and maintain a program which will locate and treat all cases of syphilis and gonorrhea among industrial workers.

**How it looks to the high school girl.**

Aimee Zillmer. Wisconsin State Board of Health, Quart. Bull., Madison, 7: 3-6, July-Sept. 1943.

Of 3,351 Wisconsin high school girls answering a questionnaire, 3,005 replied that venereal diseases come more from sexual contact than from any other source, 96 percent of the girls knew that venereal disease cannot be recognized by looking at a person, and 92.8 percent of the total number questioned replied that a physician should be consulted regarding a venereal disease.

The 3,351 girls questioned were from 46 towns and cities, totaling a population of 237,861—from communities ranging from a rural town of 346 to a city of 48,765.



Talks on social hygiene have reached 90 percent of the high schools in the State. The State has always maintained a program to assist parents in their social hygiene obligations, and when asked, "Where did you receive sex information?" 67.5 percent of the girls answered "Mother" and 5.5 percent, "Father." Home, school, church, community—all contribute to the child's point of view on sex.

Ninety-four percent of the girls suggested that sex information be incorporated in "some related course" in school.

Under the subject of fun for leisure time, school functions and "just riding around" headed the list, with home games as second choice. Seventy-five percent claimed that their towns did not have enough places for good, decent fun.

Rural and urban points of views were similar in reference to the girls' standards. When asked, "Do you think a girl should phone a boy for a date?" only 1 out of 26 or 27 answered in the affirmative.

While some of the answers were discouraging, others were good. All revealed a desire for help, a desire sometimes hidden behind a stubborn or sophisticated front or buried even deeper in a timid and puzzled soul. All the answers are clues to adult thought. Failure to follow up the clues is evidenced by the sex mistakes of youth.

**Venereal diseases: Constitutionality of city ordinance requiring treatment of infected persons convicted of prostitution. Bureau of legal medicine and legislation. J. A. M. A., Chicago, 123: 376, Oct. 9, 1943.**

By Little Rock city ordinances, prostitution is made a criminal offense and the city health officer is required to determine whether the person convicted of prostitution has any venereal disease. If such a person is found to have a venereal disease in a communicable stage, and she fails to take adequate treatment, the health officer may commit her to an institution for treatment.

The plaintiff in this case was convicted of prostitution and ordered quarantined, after being found to have a venereal disease in a communicable stage, in the health

center maintained by the United States Government at Hot Springs. She filed a petition for a writ of habeas corpus, contending that the ordinances authorizing her detention were unconstitutional and void. The trial court granted the writ and the defendants, the city of Little Rock, the city health officer and the county sheriff, appealed to the Supreme Court of Arkansas.

The Supreme Court reversed the judgment of the trial court and remanded the plaintiff to the custody of the sheriff for isolation and quarantine. This court held that any health authority, when he believed public health required it, should commit any person who, having been found to be afflicted with an infectious disease, refused to take treatment adequate for the protection of the public health, to a place where commitment could be done without endangering the life of the patient. The court held that venereal disease was to be considered on the same basis as any other infectious disease.

**Preliminary report on local venereal diseases relative to the Puerto Rico encamped military forces. Ernesto Quintero. Bol. Asoc. méd. de Puerto Rico, Santurce, 35: 180-188, May 1943.**

Between 1919 and 1938 little attention was paid to venereal disease in Puerto Rico, with the result that in 1936 syphilis was about 2½ times as prevalent there as in continental United States. The socioeconomic conditions of the island are an important factor in the high venereal disease incidence. The overcrowding which exists among about 75 percent of the population, famine, fatigue, laxity of morals, and the concurrent excitement of war aggravate the situation. Most of the young women who are attracted by high wages offered at the construction centers near the largest towns are either prostitutes or eventually become promiscuous. The influx of thousands of young soldiers from the States with plenty of money in their pockets tremendously increases the number of sex exposures, with a corresponding increase of venereal disease among the soldiers and among the civilians.

The high rate for venereal disease among the men in the Service has been due to several factors: Prostitution is widespread on the island; liquor is in common use and easily obtainable; lack of sanitary facilities increases the hazard of exposure; there is a lack of recreational facilities at the military posts. The rate of infection has varied in different camps depending on the interest of the military officers in local conditions, and the efficiency of the local control measures.

The number of civil venereal disease clinics has been increased to 56, and their location carefully chosen. Infectious cases are kept under medical care until they are no longer a menace to society by: (1) Registration in the clinics of all promiscuous patients (4,146 have been registered, which probably represents one-third of the entire potential reservoir); (2) isolation in detention hospitals, 450 beds being available; (3) intense specific treatment every other day in the clinics and strict follow-up by field agents.

The plan for the rehabilitation of venereally infected selectees includes: (1) Each venereal disease clinic accumulates information in regard to selectees from its area. (2) The local Selective Service board reports to the health authorities the number of selectees found to have positive blood examinations. (3) The Insular Police and other agencies aid in getting the uncooperative patient to take treatment. Legal measures toward the repression of prostitution have been put into practice as far as the existing conditions permit.

During the past 3 years the venereal disease control program has been reaching the infected population, as is shown by the fact that 73 percent of all patients are 15 to 40 years of age. During January and February 1943, of 94 contacts reported by military authorities, 28 were treated in the clinics and 13 in the venereal disease hospitals. There were 1,085 investiga-

tions conducted as a result of information furnished from other sources, resulting in 236 persons being treated. During these 2 months 526 patients were hospitalized, 1,647 new patients registered at the clinics, and 41,722 treatments given. From December 1942 to March 1943, 117 contacts were reported by the military authorities to the Santurce clinic. Of these, 46 persons were located, of whom 31 were already registered, 10 were registered at a clinic, 3 were sent to a hospital. Six had been reported as contacts in other cases.

To meet adequately the extra load of the wartime demands, certain recommendations are made: More clinic sessions should be provided. Clinic space and clinic hours should meet the justifiable demands of the corresponding area. Services for male gonorrheal patients should be provided. Through the medium of the radio and the local press, publicity should be given to the facilities of the Public Health Service in obtaining health certificates for servants. Cordial and reciprocal relations with the private and charity physician, and rigorous follow-up of every reported source or contact are very necessary. Isolation facilities should be increased with the purpose of lodging continuously at least one-third of the known prostitutes. The isolation of these patients should be long enough to carry on their redirection toward better and decent living. The Insular Legislature should provide legal measures to ensure an efficient policy of repression of prostitution, to take the profits out of the business, to eliminate the interest of the exploiter and promoter. There should be legal measures to deal properly with girls under age who are engaged in prostitution. At schools there should be continuous, well organized programs of health education. A sense of responsibility toward their fellow-beings and themselves should be developed by educational work among the prostitutes.

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## **STATISTICAL SECTION**

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**Health Officers' Monthly Statement of New Cases of Venereal Diseases Reported for the  
First 4 Months of Fiscal Years 1943-44 and 1942-43, in the States, Territories, and  
Possessions**

Area	Cases of venereal diseases reported for first 4 months of fiscal years below											
	Syphilis										Gonorrhea	
	Total		Primary and secondary		Early latent		Late and late latent		Congenital			
1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	
†United States.....	149,744	175,747	24,907	25,282	40,445	44,437	63,311	78,327	4,245	5,226	101,622	89,169
Alabama.....	5,985	7,686	864	975	1,414	2,180	1,436	2,383	138	206	2,484	3,508
Arizona.....	1,044	500	238	46	274	81	404	347	45	17	603	147
Arkansas.....	2,946	4,621	406	577	1,025	1,538	1,069	1,884	73	67	1,551	1,727
California.....	10,789	9,568	1,728	1,378	2,556	2,084	5,937	5,440	330	249	10,572	7,405
Colorado.....	1,587	1,384	358	283	448	319	717	713	64	69	1,182	584
Connecticut.....	1,071	876	120	89	397	196	323	377	62	34	527	534
Delaware.....	321	296	34	44	71	86	44	114	5	6	64	73
District of Colum- bia.....	2,724	(*)	348	(*)	672	(*)	1,561	(*)	45	(*)	1,256	(*)
Florida.....	11,044	10,228	1,094	1,381	3,321	2,258	5,150	5,077	229	266	6,244	4,078
Georgia.....	6,220	10,462	1,136	1,484	2,675	4,961	2,315	3,703	192	313	4,086	5,397
Idaho.....	214	165	112	61	39	6	43	69	3	10	281	73
Illinois.....	9,454	10,053	1,167	1,073	2,299	1,915	5,782	6,814	206	251	8,537	7,449
Indiana.....	2,906	4,652	386	640	256	57	1,040	1,723	88	168	1,191	1,197
Iowa.....	(*)	982	(*)	96	(*)	300	(*)	468	(*)	41	(*)	569
Kansas.....	857	1,242	148	243	179	119	496	524	34	43	703	848
Kentucky.....	2,822	4,732	377	583	617	913	1,216	1,882	114	142	1,297	1,750
Louisiana.....	6,925	7,069	983	897	1,715	1,928	1,895	3,653	158	251	4,676	1,614
Maine.....	276	348	61	79	30	57	143	152	24	40	456	241
Maryland.....	5,755	4,931	545	358	570	393	897	525	48	89	3,147	2,268
Massachusetts.....	1,643	1,853	370	329	0	0	1,199	1,425	74	97	1,594	1,797
Michigan.....	6,303	4,677	851	604	1,584	920	2,659	1,974	166	203	3,875	3,312
Minnesota.....	881	1,195	85	73	93	117	631	928	49	51	693	539
Mississippi.....	9,161	13,952	3,187	3,436	2,549	4,747	3,032	5,232	393	537	10,285	11,390
Missouri.....	3,213	3,645	608	543	797	777	1,452	1,761	111	116	1,810	1,578
Montana.....	137	214	42	71	12	13	63	106	3	3	146	97
Nebraska.....	432	694	73	76	255	140	70	424	17	23	603	571
Nevada.....	305	306	8	(*)	49	(*)	222	(*)	10	(*)	140	99
New Hampshire.....	63	109	9	10	25	12	24	72	2	8	63	69
New Jersey.....	3,944	4,116	472	461	1,308	998	2,013	2,496	147	125	1,977	2,343
New Mexico.....	694	752	155	132	156	132	341	432	42	38	496	187
New York.....	13,116	12,270	1,896	1,159	2,249	2,059	8,469	9,054	365	444	6,715	5,927
North Carolina.....	4,088	6,340	1,065	1,383	1,607	2,572	1,331	2,198	85	187	3,293	3,753
North Dakota.....	95	129	29	17	18	24	32	55	4	11	105	95
Ohio.....	(*)	7,901	(*)	1,068	(*)	1,800	(*)	4,668	(*)	365	(*)	1,766
Oklahoma.....	(*)	3,575	(*)	501	(*)	1,159	(*)	1,150	(*)	106	(*)	1,432
Oregon.....	741	523	209	94	56	54	467	331	9	44	741	386
Pennsylvania.....	4,560	1,934	570	438	1,861	1,357	1,674	13	226	25	371	(*)
Rhode Island.....	365	427	23	9	36	36	273	318	7	16	274	128
South Carolina.....	5,900	6,107	1,190	1,315	2,534	2,395	1,912	2,143	149	171	2,298	2,041
South Dakota.....	168	158	32	31	27	62	74	51	14	6	149	106
Tennessee.....	6,496	7,900	927	994	2,667	2,462	2,681	4,163	144	204	5,750	3,581
Texas.....	8,042	18,330	1,075	1,143	2,819	3,425	3,001	5,529	216	409	3,885	5,999
Utah.....	325	206	79	70	44	25	195	106	7	4	220	283
Vermont.....	89	101	26	59	24	0	37	39	2	3	65	72
Virginia.....	4,970	7,218	1,563	2,088	1,822	2,505	1,378	2,352	102	149	4,458	2,676
Washington.....	1,506	1,357	273	184	386	164	601	836	50	49	2,954	1,987
West Virginia.....	1,434	1,915	225	267	178	346	271	569	32	79	897	881
Wisconsin.....	370	344	70	57	0	0	296	285	4	2	456	237
Wyoming.....	487	162	46	48	52	4	228	55	12	1	79	139
<i>Territories and Possessions</i>												
Alaska.....	31	61	18	14	6	27	3	14	1	3	137	197
Hawaii.....	289	328	59	112	34	40	178	137	17	16	524	569
Puerto Rico.....	6,836	3,396	637	707	1,389	515	2,174	1,263	828	602	1,345	1,108
Virgin Islands.....	78	81	18	24	44	40	12	13	4	4	126	62
†Actual total of United States, Territories, possessions.....	168,857	194,296	27,245	28,002	44,907	48,711	71,616	86,990	5,479	6,408	108,487	95,825

\*Data not available for all or part of period.

1 Based on 45 States.

†Based on States reporting in both fiscal periods.

2 Based on 44 States.

Includes all reported cases.

# Health Officers' Monthly Statement of New Cases of Venereal Diseases Reported for the First 4 Months of Fiscal Years 1943-44 and 1942-43, in Cities of 200,000 Population and Over

City	Cases of venereal diseases reported for first 4 months of fiscal years below											
	Syphilis										Gonorrhea	
	Total		Primary and secondary		Early latent		Late and late latent		Congenital			
1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	
†Total.....	1 50,028	1 50,768	1 6,117	1 5,222	1 10,629	1 9,487	1 22,272	1 25,200	1 957	1 1,135	1 25,664	1 23,960
Akron.....	330	483	41	84	81	88	192	287	16	24	123	100
Atlanta.....	1,136	1,270	248	427	343	402	534	434	13	7	402	370
Baltimore.....	4,688	3,448	420	228	386	214	690	329	27	17	1,146	1,232
Birmingham.....	1,833	2,340	115	215	498	726	435	568	30	76	189	355
Boston.....	611	675	133	101	0	69	381	439	11	26	453	485
Buffalo.....	621	616	68	44	106	7	431	545	16	20	295	272
Chicago.....	4,720	6,702	743	817	1,196	1,313	2,667	4,387	114	185	4,562	5,150
Cincinnati.....	1,118	1,099	146	112	(*)	(*)	(*)	(*)	(*)	(*)	371	330
Cleveland.....	1,414	1,337	230	227	480	324	671	740	33	46	496	601
Columbus.....	526	466	91	59	109	97	291	294	15	16	117	174
Dallas.....	831	1,253	166	137	167	210	491	895	7	11	267	463
Dayton.....	664	414	62	72	190	68	386	256	26	16	215	101
Denver.....	736	716	(*)	123	(*)	118	(*)	438	(*)	25	634	336
Detroit.....	4,444	2,910	521	379	1,363	729	2,480	1,740	80	62	2,109	1,793
Honolulu.....	177	217	34	100	23	28	107	76	13	13	379	459
Houston.....	653	1,573	106	128	232	613	292	770	23	62	801	263
Indianapolis.....	(*)	1,307	(*)	230	(*)	52	(*)	450	(*)	12	(*)	318
Jersey City.....	205	277	19	22	44	44	138	201	14	10	17	25
Kansas City.....	629	769	105	107	98	98	396	492	28	34	331	316
Los Angeles.....	3,878	2,928	458	0	1,044	1,040	2,264	1,799	112	89	1,667	1,722
Louisville.....	881	841	116	109	158	147	361	438	7	20	316	533
Memphis.....	2,322	2,367	204	188	1,122	730	968	1,416	28	22	2,076	849
Milwaukee.....	163	184	19	25	0	0	133	156	1	3	81	47
Minneapolis.....	230	313	45	31	39	51	140	232	5	9	276	234
Newark.....	761	993	94	112	202	230	449	632	16	19	316	437
New Orleans.....	(*)	1,569	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	374
New York.....	9,057	9,420	1,507	1,164	2,020	1,732	5,221	5,809	225	238	4,703	4,069
Oakland.....	517	339	60	40	122	81	322	198	10	11	391	283
Oklahoma City.....	(*)	568	(*)	72	(*)	175	(*)	156	(*)	11	(*)	287
Omaha.....	203	408	16	43	140	70	33	271	14	13	191	276
Philadelphia.....	(*)	1,141	(*)	133	(*)	3	(*)	911	(*)	14	(*)	59
Pittsburgh.....	2,891	2,680	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	0	80
Portland.....	345	264	81	54	22	17	242	176	0	17	310	200
Providence.....	178	225	44	5	9	17	113	179	4	6	60	51
Rochester.....	81	92	14	2	7	1	57	82	3	7	98	74
St. Louis.....	(*)	2,033	(*)	252	(*)	640	(*)	1,068	(*)	73	(*)	549
St. Paul.....	110	195	14	16	22	25	64	141	3	6	117	73
San Antonio.....	393	579	43	57	102	139	230	349	16	24	439	322
San Diego.....	465	369	37	48	123	102	285	215	17	3	300	272
San Francisco.....	1,055	1,158	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	731	1,050
Seattle.....	443	450	50	47	90	50	269	322	8	4	533	447
Syracuse.....	364	203	9	7	16	1	327	190	12	5	106	41
Toledo.....	355	195	58	15	75	24	212	142	10	14	46	75
Washington, D. C.....	2,724	(*)	348	(*)	672	(*)	1,561	(*)	45	(*)	1,256	(*)
†Actual total.....	58,115	59,566	7,051	6,230	12,075	10,833	25,860	28,983	1,072	1,307	27,882	26,545

\* Data not available for all or part of period.

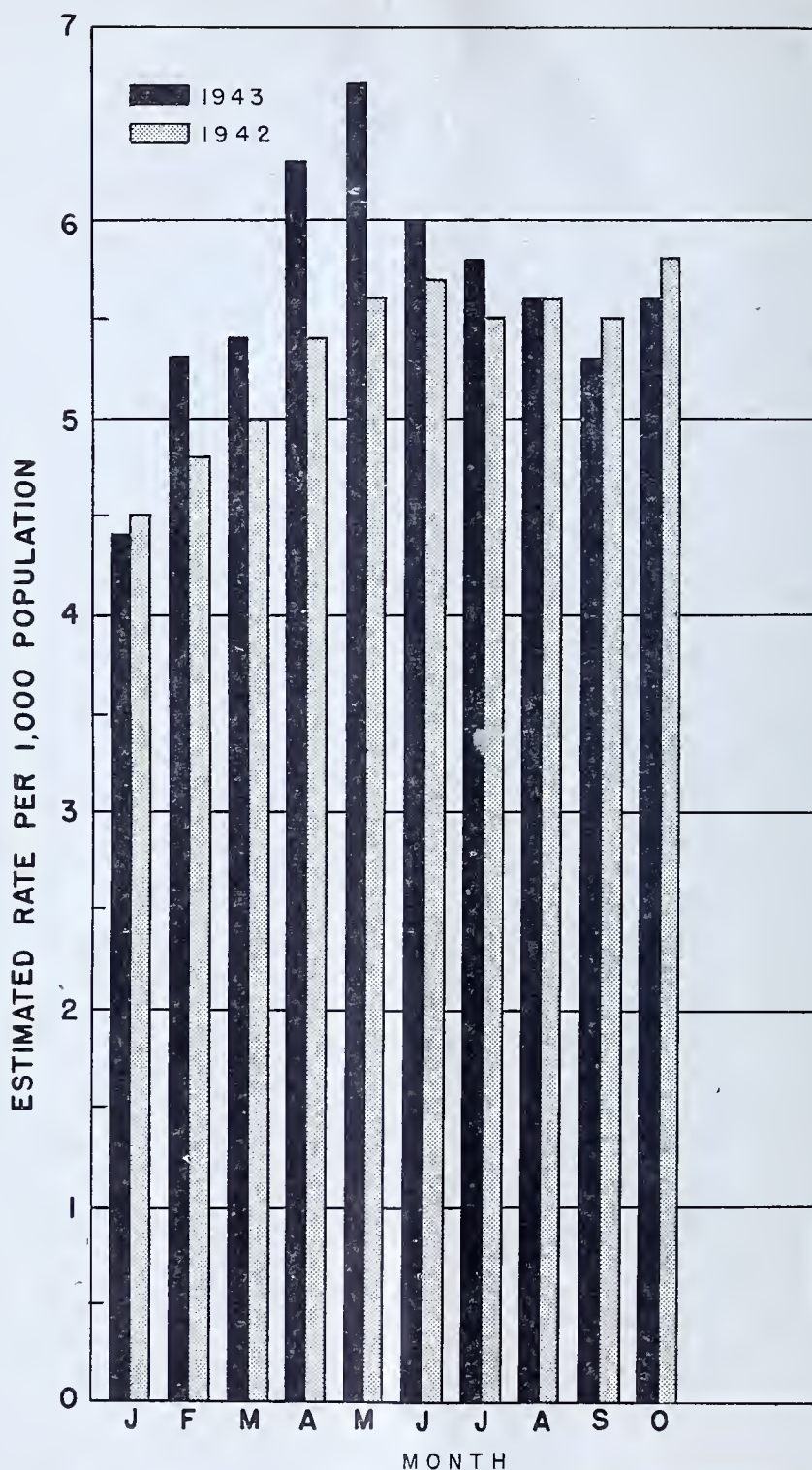
† Based on cities reporting in both fiscal periods.

‡ Includes all reported cases.

1 Based on 38 cities.

2 Based on 35 cities.

3 Based on 34 cities.



ANNUAL SYPHILIS CASE RATES  
IN CITIES OF 200,000 POPULATION AND OVER  
BASED ON PROVISIONAL MONTHLY DATA  
1943 AND 1942



# Venereal Disease Information

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THOMAS PARRAN, *Surgeon General*

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## Criteria of Cure in Gonorrhea

Richard A. Koch, M. D., M. P. H.,<sup>1</sup> Earl N. Mathis, M. D.,<sup>2</sup> and Jacob C. Geiger, M. D.<sup>3</sup>

Some years' experience with a steady, large volume of patients infected with gonorrhea has caused the authors' concern as to the validity of the ordinarily accepted criteria of cure for this infection. The patients considered in this report are those who have been treated in a large municipal public health clinic from Jan. 1, 1941 to July 1, 1943, and include both men and women with gonococcal infection. The concern has been occasioned by the repeated occurrence of positive gonococcal cultures in individuals who have become promptly asymptomatic on treatment and have remained so for long periods of time.

Positive cultures in these asymptomatic persons have been found among our patients as well as among patients who had been treated by other agencies, both private and institutional, and had been discharged as cured by them. In many instances these asymptomatic individuals have been named as sources of new gonococcal infections and have subsequently reached our attention through public health channels. Moreover, personal conversations with health officers, private physicians and military medical officers, who often are not in a position to check sources of infection or to do follow-up cultures, have frequently indicated that there is a considerable tendency to place too much faith in the asymptomatic state following antigonococcal sulfonamide treatment. Some writers (1, 2, 3, 4, 5) infer that it is unnecessary in acute an-

terior gonorrheal urethritis to perform a long series of culture rechecks on patients who have become asymptomatic and upon whom negative cultures are found shortly after the termination of sulfonamide therapy.

We feel that such criteria of cure are unsatisfactory and that an observation period of at least 3 months is required to give reasonable assurance of the elimination of the gonococcus in treated patients. Even with this conservative program for the criteria of cure, some patients will continue to harbor the gonococcus despite the absence of symptoms and the securing of consecutively negative gonococcal cultures (6). We believe that there has been inadequate comment in the literature on the importance of this phase of management; however, some writers have spoken emphatically in accordance with our beliefs (7, 8).

We have undertaken to review our total cases of gonorrhea in the adult during the period considered and to review the literature relative to criteria of cure in gonococcal infection. In general, recommendations for criteria of cure tend to fall into three general classifications. The first is that group which, in our opinion, tends to have such minimal criteria that adequate estimation of the elimination of the gonococcus is generally not possible (2, 3, 9, 10, 11, 12, 13, 14, 15, 16). The second general group is that which requires a minimal observation period of about 3 months, during which time the patient is frequently subjected either to gonococcal slide or to culture examination (17, 18, 19, 20, 21, 22). The third group represents those who either require even more stringent criteria of

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cure or who request unusual criteria frequently not recognized by the majority of medical opinion as being practical in general gonorrheal management (23). Unfortunately, some writers on the subject of the management of gonorrhea have omitted from their reports an outline of their criteria of cure.

#### EXAMINATION AND TREATMENT

The total number of adult patients observed and given treatment during the period covered by this report was 926. This does not include patients who were examined, diagnosed, and referred to other agencies before treatment was instituted. This group represents slightly more than half of those patients examined and diagnosed during this period.

The diagnosis of chronic gonorrhea, as opposed to acute, has been arbitrarily defined by us as an infection which has existed for 3 months or longer. It must be admitted that certain of these figures may not be strictly in accord with our definition of chronicity. For example, if an individual who gave the history of a diagnosis of gonorrhea 4 or 5 months previously, with minor signs and symptoms existing until the time of registration, revealed an acute epididymitis upon our examination, it is likely that the formal diagnosis would be "acute gonorrheal epididymitis," and for the purposes of this report he would be scored under "acute gonorrhea"; whereas, according to the classification based on duration of infection, he should actually have been considered "chronic." It is thought, however, that this percentage of error is very small and that it is probably fairly constant among similar statistical reports.

The diagnostic routine on the male patients was the demonstration of gonococci by spread or culture, or both, from urethral discharge; or, when a urethral discharge was not present or was negative for gonococci after a period of time, by the demonstration of gonococci in a culture of prostatic fluid. In the female patient, urethral and cervical spreads and cultures were routinely taken on the first examination in most instances, and diagno-

sis depended upon demonstration of gonococci in one of these preparations. However, no female patient who had been reported as a source or contact in gonorrhea was discharged as not having gonorrhea until 3 consecutive negative spreads and cultures, taken not less than 1 week apart, had been secured. Of the 926 patients only 6 who had negative slides and cultures were diagnosed clinically as having gonorrhea, a figure which, in retrospect, we feel is probably too small (6, 24, 25).

The laboratory work was done in the clinic laboratory by public health bacteriologists who were licensed by the California State Department of Public Health and experienced with gonococcic cultures. The material for culture was secured on a sterile cotton-tipped applicator and immediately immersed in 0.5 to 1.0 ml. of nutrient broth and placed in an incubator held at 35° to 36° C. (26). The time between securing the specimen and its placement into the incubator was generally 2 or 3 minutes. Within 1 to 2 hours, the inoculated nutrient broth was streaked on culture plates and incubated 48 hours at 35° to 36° C. in a moist atmosphere of approximately 8 percent carbon dioxide tension (27). After incubation the culture plate was flooded with p-aminodimethylaniline monohydrochloride (27) and oxidase-positive colonies were examined morphologically and tinctorially for gonococci. The laboratory was prepared to confirm all questionable colonies with sugar fermentation tests.

The nutrient broth used was Difco proteose-peptone No. 3, slightly enriched with glucose and diluted with about equal parts of ascitic fluid. More recently the laboratory has employed Nile Blue A as an inhibiting factor for saprophytic organisms in this broth (28). The plate media was composed of one-third proteose-peptone agar, one-third beef hemoglobin solution, and one-third sterile ascitic fluid. Since July 1943, tyrothricin has been added to the plate media in a dilution of 1:15,000 to inhibit the overgrowth of commensal organisms (29).

During the treatment of this series of patients, several of the sulfonamides were

employed and three different plans of administration were used as knowledge of sulfonamide therapy progressed. Of the initially started sulfonamide courses, 98 were with sulfanilamide, 817 with sulfathiazole, 8 with sulfadiazine, and 3 with sulfapyridine. Subsequent courses of sulfonamide were occasionally of a different variety from that originally given. In the earlier period covered by this report, when sulfanilamide was still being used, the dosage employed was between 450 and 500 gr. given in about 2 weeks. The other sulfonamides were given in two dosage schemes, the 828 patients so treated being about equally divided between them. The first consisted of 1 gm. of sulfathiazole given 4 times daily for the first 24 hours and a subsequent dose of 0.5 gm. 4 times daily, the patient receiving a total of 20 gm. over a 9-day period. More recently we have been giving the patient 1 gm. of the drug 4 times daily for 5 days, under which plan there is also a total of 20 gm. administered.

Antigonorrheal management has consisted not only of sulfonamide therapy but also adjunctive treatment in certain instances. In male patients remaining symptomatic following an initial course of sulfonamide therapy, local urethral treatment was given. Usually such treatment consisted of instillation twice daily of 4 cc. of 0.5 percent protargol solution or a 5 percent solution of a weak silver proteinate such as silver nucleinate, argyrol, or solargentum into the anterior urethra for a period of 5 minutes. In persistently symptomatic cases "through and through" intravesical irrigations of 1:8,000 potassium permanganate solution was rather frequently used early in this series, but recently it has seldom been

employed. In some instances, in chronic gonorrhea where satisfactory results did not appear to be forthcoming, gonococcus vaccine has been used. Fever therapy has consistently been employed in cases where the patient was refractory to other forms of treatment.

During this time our criteria of cure for both male and female patients have been:

1. Consistently negative physical and laboratory findings for a period of not less than 3 months prior to discharge from medical observation.

2. A minimum of three consecutive negative gonococcic cultures taken not less than 1 week apart. The culture material consisted in the male of prostatic fluid, and in the female of a combination of urethral and cervical secretions.

3. Generally the employment of at least one of the so-called "tests of cure," such as the passage of a urethral sound or the instillation of a small amount of 1 percent silver nitrate solution into the posterior urethra. Should there be a continuation of subjective complaints or minor physical findings, such as shreds in the urine, an occasional "morning drop," cervical discharge, chronic cervicitis or pelvic complaints, despite a minimum of 3 months of persistently negative laboratory reports, the patient was referred to other agencies for urologic or gynecologic evaluation and management.

#### STATISTICAL ANALYSIS

The stage of gonorrhea, the sex of the patient, and the number of patients with no previous history of the disease is shown in table 1. It should be noted that 60 percent of these patients had no previous history of gonorrhea.

TABLE 1.—*Stage of gonorrhea at time of diagnosis by sex*

Sex	Acute		Chronic		Total		No previous history of infection *	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Male.....	504	87. 8	70	12. 2	574	100. 0	291	50. 7
Female.....	222	63. 1	130	36. 9	352	100. 0	264	75. 0
Total.....	726	78. 4	200	21. 6	926	100. 0	555	59. 9



A statistical analysis of the disposition of the 926 patients under consideration is given in table 2. It is shown that 358 cases (39 percent) were closed as cured upon the basis of our criteria of cure. The largest other factor influencing the disposition of patients is the lapsed cases, which include 400 patients, or 43 percent of the total group. It will be noted that

about half of the patients who lapsed were asymptomatic; a majority of these cases were about to be closed as cured. Prolonged medical observation of patients with gonorrhea will increase the clinic lapse rate. This is especially true in a community such as San Francisco which has a large transient population.

TABLE 2.—Disposition of gonorrhea patients

Disposition	Male		Female		Total	
	Number	Percent	Number	Percent	Number	Percent
Cases closed as cured.....	204	35.5	154	43.7	358	38.7
Lapsed:						
Symptomatic.....	157	27.4	47	13.4	204	22.0
Asymptomatic.....	114	19.9	82	23.3	196	21.2
Transferred to private physician or other clinic.....	99	17.2	69	19.6	168	18.1
Total.....	574	100.0	352	100.0	926	100.0

At the time of their original registration a significant proportion of these patients had been in this community for only a short time, frequently only a few days. In many instances the infection had been acquired either before their departure for or during their trip to this community. Many of these patients, upon becoming asymptomatic, traveled to other communities or engaged in the merchant marine shipping; therefore, we were unable to continue clinic observation. It will be noted that 18 percent of patients upon whom treatment was begun were referred to other treatment agencies before treatment was completed. This figure includes those who became financially ineligible after treatment was instituted, those who moved to another community, and those who did not respond to clinic management with sulfonamides and were referred for fever treatment.

Table 3 presents an analysis of 381 patients, diagnosed as having acute gonorrhea, who became asymptomatic following one course of sulfathiazole therapy. Uncomplicated, early, acute gonorrhea (anterior urethral in the male and urethral or cervical in the female) treated initially with sulfathiazole was selected for table 3 for the express purpose of eliminating as many intangible and variable fac-

tors as possible. Of these 381 patients with acute, uncomplicated gonorrhea, 132 gave a past history of gonorrhea and 249 denied having had a previous infection.

It is of interest to note that of these 381 patients, 125 (33 percent) were found to have positive gonococcic cultures at some time within 3 months following sulfathiazole therapy and after they were clinically asymptomatic. A previous history of gonorrhea did not affect unfavorably these treatment failures. Twenty-five percent of those patients who became clinically asymptomatic and had a previous history of gonorrhea were found to have positive cultures. In contrast to this group, 37 percent of those patients who became clinically asymptomatic and had no previous history of gonorrhea were found to have positive cultures. These statistics definitely indicate the fallacy of accepting freedom from clinical symptoms as an adequate criterion of cure even in the patient who reacts most favorably to the sulfonamides, and in whom one would expect the most favorable conditions for complete cure with one course of the drug. It is definitely our opinion, therefore, that only carefully secured laboratory specimens properly cultured, examined, and repeated at safe intervals should be accepted as tests of cure in the clinically



asymptomatic patient. It is necessary to emphasize the importance of securing the specimens carefully, especially in the female where the urethra should be properly massaged, the cervical, plug com-

pletely removed, the cervix squeezed firmly between the blades of the speculum, and a specimen secured from the direct discharge of Skene's glands and the cervical glands (24).

TABLE 3.—Analysis of 381 patients with acute uncomplicated gonorrhea who became asymptomatic following one course of sulfathiazole

	Total cases	Positive culture after becoming asymptomatic	
		Number	Percent
Previous history of gonorrhea:			
Male.....	105	23	21.9
Female.....	27	10	37.0
Total.....	132	33	25.0
No previous history of gonorrhea:			
Male.....	129	41	31.8
Female.....	120	51	42.5
Total.....	249	92	36.9
Total:			
Male.....	234	64	27.4
Female.....	147	61	41.5
Total.....	381	125	32.8

Table 4 analyzes all patients with gonorrhea, irrespective of stage or previous history of disease, who were found to have a positive gonococcic culture after having become asymptomatic following sulfonamide therapy. The majority of these patients had sulfathiazole for their initial therapy. It will be noted that of the 926 patients under consideration 640 (69 percent of the total) were clinically without subjective complaint or positive physical findings after treatment with sulfonamides. The remainder of the patients (31 percent) were discharged as symptomatic either because of having lapsed from treatment without permission or because of referral to a private physician or another clinic in a symptomatic state. It is significant that of these 640 patients, there were 205 (32 percent) who had a positive culture at some period during their asymptomatic state following sulfonamide therapy. The breakdown as to sex shows that 28 percent of the males and 37 percent of the females had such positive cultures. Moreover, it should be observed that, of the 205 patients having positive gonococcic

cultures after having been asymptomatic, 109 (53 percent) were found to have positive cultures more than one month after sulfonamide therapy had been terminated. The high percentage of treatment failures in our series raises considerable doubt as to the justification for claims of high percentages of cures in reports that do not include a prolonged culture follow-up period (2, 3, 11, 12, 30). These figures illustrate the importance of recognition of the existence of a carrier-state in the control of gonorrhea.

COMMENT

The statistics presented show the fallacy of accepting the asymptomatic state of a patient with gonorrhea who has been under sulfonamide therapy as sufficient evidence that the patient has been cured of his disease. It has been shown that a third of these patients are still infectious during this clinically asymptomatic state. It is reasonable to believe that 3, 4, or even 5 months of laboratory observation may not be sufficient to assure that all patients are bacteriologically negative.

It seems, however, that 3 months is a reasonable period of observation, both insofar as the ability to hold the patient is concerned and in the protection of the

public health. This is true in view of the fact that only 5 percent of the patients in our study have been found to be positive for a period of 3 months and over.

TABLE 4.—*Gonococcic culture findings on 640 gonorrhea patients who became asymptomatic after treatment with one course of a sulfonamide*

	Male		Female		Total	
	Number	Percent	Number	Percent	Number	Percent
Total cases studied.....	363	100.0	277	100.0	640	100.0
Cases with no positive culture after being asymptomatic.....	260	71.6	175	63.2	435	68.0
Cases with positive culture after being asymptomatic.....	103	28.4	102	36.8	205	32.0
Month positive culture occurred:						
0-1.....	43	41.7	53	52.0	96	46.8
1-2.....	36	35.0	33	32.4	69	33.7
2-3.....	15	14.6	15	14.7	30	14.6
3 and over.....	9	8.7	1	1.0	10	4.9

It has not infrequently been our experience that patients, especially the sexually promiscuous, who have fulfilled inadequate criteria of cure by various treatment agencies have been the sources of local epidemics of gonorrhea. It is this group, perhaps more than any other, that has contributed to a constantly increasing gonorrheal morbidity in various areas.

It has been shown that rapid clinical response to sulfonamide therapy is no criterion of bacteriologic cure. It has also been shown that absence of a history of previous gonorrhea is of no value in assuring bacteriologic cure, even in patients with acute gonorrhea who clinically respond favorably to an initial course of sulfonamide (31). We feel that those workers who have reported more than 80 percent cure of gonorrhea with the sulfonamides have failed to search exhaustively for the presence of the elusive gonococcus over a prolonged period of time. It is definitely in the interest of gonorrhea control that minimum criteria of cure be established. Such minimum criteria will be of assistance in medicolegal problems arising in the public health control of the disease.

#### SUMMARY

1. A statistical analysis of treatment results in 926 cases of gonorrhea is presented.

2. An asymptomatic state following the treatment of any stage of gonorrhea with sulfonamides is not satisfactory evidence of cure, irrespective of previous history of the disease.

3. Diligent search for gonococci over a prolonged period (3 months) will reveal their presence in 30 percent of clinically asymptomatic sulfonamide treated patients.

4. Adequate criteria of cure are of great importance to the successful control of gonorrhea.

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# Progress in the Wartime Management of Gonorrhea

PERCY S. PELOUZE, M. D.<sup>1</sup>

During the past 6 months, in which I have been serving as a full-time consultant to the Public Health Service in the study and promotion of more effective methods for the clinical management of gonorrhea, I have had many decidedly interesting experiences. Not only has my time been devoted to lecturing in the Army Service Commands and Naval Hospitals and among the civilian physicians, public health nurses, regional health officers and civic organizations, but I have been in many dispensaries where patients with gonorrhea were or should have been treated. Of course, I knew before starting this work what was right and what was wrong with what has come to be known as the "Campaign for the Control of Gonorrhea." In fact it was because of that knowledge and knowledge of what gonorrhea has meant to every war effort that I consented to close my office and devote my time to an attempt to correct what was not to the best advantage of all concerned.

In view of my unusual opportunities for studying the problem from so many angles and from such close quarters, I shall discuss "Progress in the Wartime Control of Gonorrhea" from the standpoint of a regrettable lack of progress. No one will deny some progress and no one conversant with present conditions will fail to admit that a number of things stand in the way of far greater progress. There has never been a time in our his-

tory when there was greater need for physicians to practice critical self-examination, and to correct certain deficiencies which such examination reveals. Gonorrhea is the greatest single health problem in the Armed Forces. Even with our advances in treatment, it still stands as the greatest single cause of lost man-days in the services.

Time and space will be saved if we consider separately the groups vitally concerned in gonorrhea control. In doing this, let us forget our natural sensitiveness about having our shortcomings revealed. This is a grim, stark, vicious, all-out war, in which all of us should be able to take criticism in order that faults be corrected for the common good. We all know that gonorrhea has been one of our unpleasant social secrets and has elicited little keen interest among the groups concerned with its control until war brought full realization of its importance as a saboteur of war effort. Therefore let us forget the past, and take stock of the present, so that the future may be something upon which we can look with pride.

## THE ARMED FORCES

It is among the armed services that the problem of gonorrhea is of real urgency. It is here that the most is being done about the matter. Not only are service physicians making strenuous efforts to arouse their stations to the importance of the disease, but they are today the prime stimulants of civilian control efforts in nearby areas. Realizing that years of general medical disinterest in gonorrhea prevented maximum exploitation of modern therapeutic knowledge, the services have

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welcomed teaching from the outside to the end that existing faults might be corrected. As previously stated, it has been my privilege to do a large amount of teaching in Army and Navy hospitals, and it is a pleasure to be able to say that I have never talked to more deeply interested physicians. Everywhere I have been almost overwhelmed by courtesy as well as by questions that never would have been asked had not interest been very keen. A deep determination to learn everything which would serve to help those in their care was everywhere in evidence.

#### THE PUBLIC HEALTH SERVICE

Through the provisions of the LaFollette-Bulwinkle Bill the Public Health Service has done what it could to foster gonorrhea control. Not only has it distributed funds among the States for this purpose, but it has loaned to the States well-trained officers to assist in the effort. However, the path has not always been easy, since there is no direct control of Federal funds after they pass State borders. To date, Federal venereal disease control moneys allotted to the States have been devoted mainly to syphilis control, though it has been urged that a proportion of them should be used for gonorrhea control. This fact will be discussed when consideration is given to conditions at and below the State level.

The Public Health Service has been the prime mover in efforts toward the suppression of prostitution and has thus contributed greatly to what control is in evidence around military posts. From the Surgeon General down, there is a deep determination to aid and encourage elimination of gonorrhea as a military and social menace. It faces tremendous obstacles. Below the State level there is an unfortunate lethargy toward gonorrhea against which the Public Health Service has not the power to act except through persuasion and encouragement. It does not feel that it has even the right to deny Federal funds in cases where such encouragement goes unheeded.

In the States one will search far, as a rule, before finding anything that justly could be called a campaign for the control of gonorrhea. It is here that one finds so much of the old disinterest and feeling of defeatism that has always stood in the way. Often it starts with the State health officer and pervades every level beneath him. And it is in the lower reaches of his domain that whatever he may have started as a control program fades into nothingness. So true is this that the plans of the health officer who sits in a swivel chair in the State capital and gives orders about gonorrhea control are doomed to failure. On the other hand, the officer who goes into his local dispensaries, discovers what is wrong there, and takes steps to correct the faults will have more success than he ever dreamed possible.

In those States wherein important military posts are located, efforts usually have been made toward police suppression of prostitution. Were the same care given to the medical treatment of prostitutes and to bringing under treatment the thousands of other infected civilians, far more pride could be taken in accomplishment.

Since State control is lacking at the dispensary level, it is highly important that those responsible for local activities should know just what is hampering their plans. I give you a typical example: In the first place, the dispensary was set up for syphilis control. Much effort was expended in staff education and this educational effort has been a continuing one. Then, to a group thus trained for syphilis control, orders were issued that gonorrhea also must be treated. No efforts were made to fit the workers to care for such patients. It apparently was assumed that no education was needed; that people just automatically understood gonorrhea and the folks who had it. For years the staff had read or heard that, epidemiologically, syphilis and gonorrhea were the same. The question was dropped at that point,



regardless of the fact that gonorrhea is a far more secret disease than syphilis and is taken far less seriously by those who have it; also that the gonorrheic male is the shyest of all medical patients, and is driven from treatment by the most trivial of occurrences.

Although gonorrhea occurs much more frequently than syphilis, it is indeed rare to find a dispensary treating both diseases which has a gonorrhea case load comparable to syphilis.

Down at the dispensary level and just above it most health officers, dispensary workers, and public health nurses frankly admit they know practically nothing about gonorrhea. Nor do they claim to know much about the gonorrheic patient as an individual. However, having lectured to hundreds of them, I can testify to their almost universal desire to understand. The countless numbers of sensible questions they have asked convinces me that here is the point at which any State control program should begin. A general is worse than helpless with troops that lack training. It will not do to assume that sulfathiazole answers the whole question, since at least one out of four males in dispensary practice fails to respond to it. Education is needed and wanted. And it should be education that encompasses both the disease and its relation not only to the war effort but to society at large.

#### THE MEDICAL PROFESSION

The urgency of national defense forces us physicians to honest self-examination. Most of us started practice when the disease gonorrhea was socially taboo. Many of us, particularly in the North, proudly boasted that we did not treat it. Many of us as frankly admitted that we knew little or nothing about it as a disease. In meetings where it was under discussion, our sole thought was "How do you treat it?" and not "What is the disease?" In our medical courses, as a rule, gonorrhea was given scant attention. Most of the physicians who did treat it considered only the patients,

without a thought as to the source of the disease or the patient's possible contacts. In other words, we displayed little social vision. We viewed the infected patient as a being apart from his social environment, and we refused to report his infection to our health agencies. Practically all of us must admit these things.

Time has changed all of this. Gonorrhea is no longer socially taboo and most of our past attitudes are somewhat archaic for a progressive profession. The time is here when we must hasten to erase past faults, and get ourselves in line with the march of progress. None of us is too good to treat gonorrhea and none is justified in treating it by the old haphazard ways still so commonly held. The same society that looked down upon gonorrhea as a just reward for what it called "sin" is being rapidly awakened to the enormity of this problem, and the time is here when every physician should know more about the disease itself and what it means to society than about its purely therapeutic aspects.

#### THE PUBLIC

Unquestionably the bars are down for public education and we shall not meet with a full measure of success until we have an informed public opinion to support our efforts. It has been so in the control of the other communicable diseases, and it is even more so in gonorrhea. Education is particularly needed among the poor and near-poor, for it is among them that most of the gonorrhea in civil life is found. Before we go far in this respect, however, we should look carefully at the places to which we invite the infected for treatment, as well as at the treatment they are to get. Beyond this our problem is threefold: (1) case-finding, (2) case-holding, and (3) case-curing. And none is a separate and distinct endeavor; society needs them all and should get them. They are the responsibility of physicians in private practice, just as surely as of those belonging to departments of public health.



## DISCUSSION

Though the present discussion is confined largely to what is amiss with our so-called campaign for the control of gonorrhea, it would be unfair to overlook what progress has been made. To have been given so miraculous a drug as sulfathiazole just before a war means untold progress. It means that the majority of the infected in our military forces are cured within the first 5 days of the disease, and by one course of medication. It means that some of those who fail with one course of the drug can be cured by a second. It means an enormous reduction in lost man-days due to gonorrhea. It means that in civil practice we have the same possibilities for quick cure of a large proportion of the patients who come into our hands. And, by the same token, it increases the need to get more and more

patients under treatment, for it is probable that not more than one-third of the cases of gonorrhea in any community ever apply for treatment, either in our offices or dispensaries.

The national effort to suppress prostitution, to get out of circulation that vast horde of women who expose many men each day is in the line of progress. The effort to furnish hospitalization and possible rehabilitation is certainly no reverse step. To have overcome social taboos to the extent that our newspapers can discuss frankly the so-called venereal diseases is enormous progress, which opens the door for the most strenuous efforts wherein the real truth can be told as it should be. Just what we do with all this progress is up to us. The tracks are cleared and the journey ahead can be just what we make it.

# Merthiolate as an Effective Bacteriostatic Agent in Spinal Fluid Specimens

AD HARRIS, Serologist, and J. F. MAHONEY, Senior Surgeon, United States Public Health Service

Spinal fluid specimens transported through the mail to a central laboratory for serologic testing not infrequently display evidence of gross bacterial contamination upon arrival. The proportion of specimens thus rendered unsuitable for testing is appreciable during the entire year but the loss becomes marked during the warm months. The object of this paper is to record a method which has been developed for the purpose of reducing this loss to a practical minimum.

The collection of spinal fluid specimens usually is carried out with reasonable attention to sterility. A reduction in the number of contaminated specimens through the observation of rigid asepsis at the time of collection would be difficult of accomplishment. Also the practice of filtering or centrifuging contaminated specimens at the time of testing is only a partially effective measure as these procedures do not remove the end products of bacterial metabolism which are soluble in spinal fluid. These circumstances rather indicated the need of an agent which would curtail bacterial growth without interfering with the mechanism of the usual tests for syphilis, either through chemical action or through the introduction of a dilution factor.

Of all compounds surveyed, merthiolate (sodium ethyl mercuri thiosalicylate) was found to be the most satisfactory when utilized in the following manner.

The test tube which usually is used for the transportation of spinal fluid specimens is approximately 13 x 100 mm.

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From the Venereal Disease Research Laboratory, United States Marine Hospital, Staten Island, N. Y.

Into tubes of this size is pipetted 0.1 ml. of a 1 percent solution of merthiolate. This solution is prepared by dissolving merthiolate substance in distilled water. The tubes are then placed in a vacuum desiccator over calcium chloride at room temperature and the solution evaporated to dryness. In a desiccator filled with tubes the dehydrating process may require 48 hours. The observation of sterile precautions is not necessary.

Upon removal from the desiccator the tubes are stoppered with paraffined corks. These corks are prepared by immersing new corks in hot, but not smoking, paraffin for 1 minute or less. Upon removal the corks are rolled on cloth to remove the excess paraffin. The tubes may then be stored for several months in the dark and used for the reception of spinal fluid as needed.

The concentration of merthiolate obtained when 2.0 ml. to 8.0 ml. of spinal fluids are added to these tubes has not been found to be sufficient to influence the results of Kahn, Kolmer, Kline or Eagle tests for syphilis. Comparable results were obtained by the described methods in tests carried out in a series of approximately 500 spinal fluids tested before and after the addition of merthiolate. Concentrations of 1:1,000 and 1:10,000 did not alter test findings to an appreciable degree.

## SUMMARY

A tube containing 1.0 mg. of merthiolate substance has been found efficacious in curtailing bacterial growth in spinal fluid specimens transported through the mail for serologic testing. A method of preparing the tubes is outlined.

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## DIAGNOSIS

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**Serologic reactions in nonsyphilitic individuals.** Milford E. Barnes, Irving H. Borts, Chester I. Miller and M. Pearl Spanswick. *J. Iowa M. Soc., Des Moines*, 33: 500-505, Nov. 1943.

The authors feel that too much dependence is placed on serologic reactions in the diagnosis of syphilis. During the past few years thousands of individuals have been labeled as syphilitic because of only a positive serologic reaction; they have been refused marriage licenses, rejected from the Army and from industry, and subjected to antisymphilitic treatment.

In a study of the reactions in the serums of 993 known syphilitic persons who were tested simultaneously by the Kline, Kahn, and Kolmer technics, the Iowa State Hygienic Laboratory found that 13.5 percent gave entirely negative reactions for all three tests and 9.7 percent gave contradictory reactions. The frequency of contradictory serologic reactions among reactors subjected to Kline, Kahn, and Kolmer tests ranged from 11.3 to 45 percent in various groups. These results were confirmed by at least two consecutive tests.

Contradictory reactions may persist or they may disappear without antisymphilitic treatment. The explanations offered for their disappearance are that (1) they were due to syphilis which, during the testing period, passed into a latent, non-reacting stage, (2) they were due to syphilis which, during the testing period, had undergone spontaneous cure, or (3) they were due to causes other than syphilis which ceased to exist during the testing period. The authors feel the last explanation to be the most probable and cite 14 cases to substantiate their theory. Among these 14 asymptomatic cases with contradictory reactions, complete spontaneous serologic reversal to a negative state took place after periods ranging from weeks to months. In some in-

stances this reversal was observed in persons on a low protein diet.

These findings should serve as a warning to physicians not to place their diagnoses solely upon serologic reports. It is as much their responsibility to rule out syphilis as it is to diagnose it.

### **Some principles of diagnosis in syphilis.**

C. W. Barnett. *Stanford M. Bull., San Francisco*, 1: 165-169, Aug. 1943.

The diagnosis of syphilis involves much more than a demonstration of the existence of the infection. There must be a complete appraisal of each patient, the first step in which is a careful and complete history and physical examination. The author believes this to be more important than the performance of the serologic tests. Because a large number of patients are without signs and symptoms it is customary for some physicians to omit the physical examination. This may lie back of the belief that the character of syphilis is changing. There may be some reduction in the incidence of lesions as a result of increased treatment but they still exist and are common if looked for. The more exhaustive the examinations, the higher will be the incidence of both early and late lesions and the lower the number of latent infections. Data obtained through the Central Tabulating Unit of the U. S. Public Health Service concerning the diagnoses made in the clinics in six western States in 1942 showed the incidence of diagnosis of latent syphilis to the frequency of physical examination was 69 percent, while for the Stanford Clinic it was 45 percent; for syphilis with lesions the rates were 31 and 55 percent, respectively.

The author feels that in the campaign to publicize venereal diseases too much stress has been placed on the serologic reactions at the expense of an understanding of the disease itself. In proving the presence or absence of the infection, the



serologic tests are invaluable, but they are useless in the evaluation of several other factors essential in a complete diagnosis.

It is essential that a sharp distinction be drawn between the serologic tests that are strongly positive and those that are partially positive. The physician should consider as doubtful all partial positives and all instances in which there is a disagreement between different tests. They may be accepted as confirmatory in patients with physical evidence of syphilis but should be viewed with suspicion when they are the only evidence of infection. Careful consideration should be given to the probability of exposures, to healthy marital partners and children, and particularly to the possible existence of any intercurrent disease that might cause a positive reaction. When the usually more sensitive tests are less strongly positive than weaker ones, suspicion of a false positive reaction should be aroused.

The most important factor in the interpretation of weakly positive reactions is prolonged observation. Many physicians erroneously regard the treatment of all types of syphilis as an emergency measure.

The author emphasizes that treatment should never be administered until all diagnostic measures that are necessary to fully establish the presence of the infection and the stage of the disease have been completed.

**Prostatitis and seminal vesiculitis; acute and chronic.** Roy B. Henline. J. A. M. A., Chicago, 123: 608-615, Nov. 6, 1943.

The author believes that chronic prostatic infections occur with greater frequency than is generally believed. The manifestations may be so capricious that it becomes a matter of chance during routine examination to discover the prostate as the source of infection. Acute prostatitis and seminal vesiculitis usually develop from an active infection in the posterior urethra. The offending organism may be the gonococcus, but any other pyogenic bacteria can produce an acute prostatic infection.

Chronic prostatic infections, in most instances, are not caused by the gonococcus. Gram-positive cocci are frequently mistaken for gonococci, both in urethral and in prostatic spreads, and a diagnosis of gonorrhea is erroneously made. Gonococci should be searched for with extreme care before the diagnosis of gonorrhea is made. The author believes that it is unfortunate that patients as well as practitioners are of the opinion that chronic prostatitis is preponderantly due to, or the result of, gonorrheal urethritis. This point of view often does an injustice to many patients suffering from chronic prostatitis. A certain percentage of cases of chronic prostatic infection results from gonorrhea, even though the gonococcus cannot be demonstrated in the prostatic secretions. Frequently more than one type of organism is found; in a series of 170 cultures, 60 contained two or more organisms, while 22 failed to reveal any bacteria.

**Pinta (mal del pinto, carate) in continental United States. Report of three cases with late manifestations and review of the salient features of the disease.** E. P. Lieberthal. J. A. M. A., Chicago, 123: 619-624, Nov. 6, 1943.

Pinta is a nonvenereal type of spirochetosis limited almost exclusively to the dark races. The initial lesion appears on the cutaneous surface at the exact site of entrance of the causative organism, *Treponema carateum*, after an incubation period of 7 to 20 days. In 5 months to a year the secondary lesions, or pintids, appear. In the terminal stage achromic and hyperpigmented spots and atrophy of the skin are encountered. In this stage the complement fixation and precipitation reactions are strongly positive and adenopathy may be present.

Pinta has never been reported in continental United States. However, there are probably cases of pinta in the Southern States which have been diagnosed as vitiligo, postsyphilitic dyschromia, or residual

achromia secondary to various inflammatory dermatoses.

In 1926 Menk of the United Fruit Company reported that the Wassermann reactions of 74.6 percent of his patients with pinta were positive, and in 1927 González Herrejón found that almost all of his patients had strongly positive reactions although they presented no evidence of syphilis. León y Blanco established the relationship of pinta to frambesia and to syphilis by his experiments in Mexico and Cuba.

During the secondary stage of the disease, which may last a year or more, the Wassermann and Kahn reactions have been found positive in only 60 percent of the cases. The general health is never affected. The secondary stage lasts from several months to more than a year. The lesions become dyschromic, and the resulting clinical picture is that of vitiligo. The pigmented lesions of the third stage are coffee color, slate blue or jet black according to the darkness of the normal skin. In the late stage hypertension, cardiovascular lesions and changes in the spinal fluid are observed.

The treatment of pinta is similar to the treatment of frambesia and of syphilis. Arsenicals administered intravenously and bismuth and mercury compounds intramuscularly are specific. The Wassermann and Kahn reactions may remain persistently positive in spite of intensive and prolonged treatment. The treatment should be continued until serologic reactions are negative. When these reactions remain positive in spite of treatment, fever therapy or treatment with nonspecific proteins, followed by therapy with heavy metals, is worthy of consideration.

The authors discuss at length 3 cases of pinta which they have seen. Pardo-Castello studied these cases and agreed that in two of them the disease was exactly the form seen in Cuba, and the other that seen in Mexico, Columbia, Ecuador, and Venezuela.

Case 1 was that of a woman, 51 years old, who had been born in Ontario of mixed Indian, French and Negro parentage, and had lived in Pittsburgh and

Chicago since she was 3 months old. She had a generalized pruritus and "white spots" on the skin, and there were lesions of a peculiar bluish black. She had received two courses of treatment with bismuth salicylate. The results of additional antisyphilitic therapy were striking.

Case 2 was that of a Negro woman, 51 years of age, who was born in Louisiana and went to Chicago in 1939. She had had 7 spontaneous abortions. She had received a course of neoarsphenamine and bismuth salicylate. When she was admitted to the hospital, her blood reactions were strongly positive, and they remained so for 2½ years in spite of continuous treatment. The cutaneous response to therapy was rapid.

The third patient, a Negro aged 50, had been born in Alabama, but had recently moved to Chicago. In 1939 examination revealed cardiovascular syphilis but no involvement of the central nervous system. There was no history of syphilitic infection. A hyperpigmented area was seen on the right wrist and juxta-articular nodes were present on the right hand and right knee. In May 1940, after 3 courses of treatment with bismuth salicylate, the pigmented patch and the nodes had disappeared. On Aug. 8, 1942, the patient was admitted to the hospital, acutely ill, and he died on August 24. No evidence of syphilis was found at autopsy, but there was general arteriosclerosis, hypertrophy and dilatation of the heart, and a small aneurysm of the right coronary artery.

All 3 patients maintained that they had never had sexual relations or shared living quarters with persons who had lived in the tropics or who had lesions resembling theirs.

**Bubonulus in granuloma inguinale.** Nathan Sobel and Nathan Pensky. Arch. Dermat. & Syph., Chicago, 48: 494-496, Nov. 1943.

Granuloma inguinale is a disease which is almost always limited to the skin and does not as a rule affect the lymphatics. The case which is reported, however, shows that the lymphatics may be in-



volved, and the authors suggest that if very early cases were carefully observed a higher incidence of lymphatic involvement with bubonuli might be found.

The patient was a Negro, 20 years of age, who came to the clinic complaining of painless sores on the penis, which had first appeared as pimples 3 weeks earlier. There were several lesions on the penis and two fluctuating abscesses. On pressure over both abscesses a thin yellowish pus was expressed which appeared on the surfaces of the ulcers below, thus showing a communication between the abscesses and the ulcerations. Donovan bodies were easily demonstrated in the pus, but tests for chancroid, for syphilis and for lymphogranuloma venereum all gave negative results.

One week after admission the inguinal lymph nodes became moderately enlarged but not tender and they did not suppurate. There was no change after the patient had received 14 gm. of sulfathiazole. He was then given intravenous injections of 1 percent aqueous solution of antimony and potassium tartrate in 5 cc. doses 3 times a week. After 17 such injections over a period of 12 weeks, the lesions were almost completely epithelialized.

**The differential diagnosis of lymphogranuloma venereum and chancroid by laboratory and skin tests.** Leslie W. Knott, Leo H. T. Bernstein, Harry Eagle, Terrence E. Billings, Robert L. Zobel and E. Gurney Clark. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, 27: 657-685, Nov. 1943.

The authors conducted this study to determine the utility of the Ito-Reenstierna test, the Frei test, the lygranum skin test, the lygranum complement fixation test, and changes in the serum protein and in the serum albumin-globulin ratio, in the differentiation of chancroid and lymphogranuloma venereum.

All patients in the study with genital lesions suggesting a venereal disease were referred to the syphilis clinic and those in whom the darkfield examination showed no *T. pallidum* were placed on special observation and treatment.

Nearly all the patients were Negroes. A control group was composed of 20 white members of the staff personnel. Every patient received repeated darkfield examinations and repeated serologic tests for syphilis. Complement fixation tests for lymphogranuloma venereum using the "lygranum" antigen were also performed. All patients whether diagnosed as lymphogranuloma venereum or chancroid received sulfadiazine, 4 gm. daily, for a period of 2 to 3 weeks. There were 44 patients with genital lesions diagnosed as chancroid and 31 as lymphogranuloma venereum, and 18 patients were placed in the miscellaneous group. The various tests to be studied were carried out on each group and tables are given which analyze the results.

The conclusions of the authors from this study are: The results of the diagnostic skin tests (Ito-Reenstierna, Frei and lygranum) for chancroid and lymphogranuloma venereum should be interpreted with caution. A positive reaction does not necessarily establish the diagnosis nor a negative reaction exclude it.

The specificity of the lygranum complement fixation test is challenged by the large number of positive reactions found in the serums of patients giving no history and presenting no clinical signs of the disease and also by the possible cross-reactivity with other venereal diseases, particularly syphilis.

In a case of syphilis, the initial results of the lygranum complement fixation procedure are unreliable and the test should be repeated throughout the course of anti-syphilitic therapy.

Biologic false positive tests for syphilis occur with surprising frequency in cases with chancroid, lymphogranuloma venereum and other types of nonsyphilitic genital lesions. It is therefore emphasized that arsenical therapy should not be initiated in a patient with a darkfield negative genital lesion and a low titered serologic test for syphilis, even if the results are confirmed by repeated tests. Following the reagin titer in repeated quantitative tests is of value in such cases.



The determination of the total serum protein and albumin-globulin ratio is of little value in the differential diagnosis of genital lesions.

The best criterion in the differential diagnosis of chancroid and lymphogranuloma venereum remains the clinical appearance of the lesion. The skin reactions and serum tests are at best of confirmatory value, but do not alone suffice to establish a diagnosis.

**Observations on the specificity of the Frei test in Army personnel using lygranum as antigen.** Abraham Gelperin. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, 27: 697-699, Nov. 1943.

Frei tests, using lygranum as antigen, were carried out on 192 enlisted men in two Negro platoons and 166 white men of the Station Complement at Camp Claiborne, La. Both groups had recent negative blood tests for syphilis and no evidence of venereal disease. Addresses for 5 years prior to induction were obtained from each man, and it was found that there was no statistically significant difference in the percent of positive Frei tests in soldiers from northern and southern States.

The incidence of positive Frei tests in the Negro troops was 18.7 percent and in the white 1.2 percent. Neither of the two white men who had positive tests had a history of any venereal disease. A tabulation according to history of past infection showed that 52.6 percent of the Negro and 8.4 percent of the white men had a history of gonorrheal infection. When the groups of Negro soldiers with a history of penile lesions other than uncomplicated gonorrhea were consolidated, the percentage of positive Frei tests was 42.8.

Frei tests were performed on another group of 29 Negro soldiers who had been in the hospital because of penile lesions not diagnosed as chancroid, syphilis or lymphogranuloma venereum. Fifteen had painless, slightly enlarged inguinal lymph nodes in addition to the penile lesion. Reexamination 2 to 8 weeks after discharge from the hospital revealed no evidence of disease, and 43.3 percent had

positive Frei tests. The author says that, granting the specificity of lygranum, it is obvious that there is a considerable latent mild infection with the virus of lymphogranuloma venereum in the Negro.

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## TREATMENT

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**Further observations on penicillin in sulfonamide resistant gonorrhea.** E. N. Cook, T. L. Pool and W. E. Herrell. *Proc. Staff Meet., Mayo Clin., Rochester*, 18: 433-437, Nov. 17, 1943.

The use of penicillin has continued to prove an exceedingly effective agent in the treatment of sulfonamide resistant gonococcic infections. The authors report their results on 10 male and 3 female patients, all of whom had failed to respond to sulfonamide therapy. One additional patient who had not received sulfonamide also improved under this treatment. In all 14 cases chocolate blood agar cultures were positive for *Neisseria gonorrhoeae* before treatment.

Satisfactory results from the penicillin treatment were obtained in all of the 14 cases. In the 11 male patients negative cultures were obtained between 14 and 48 hours after the beginning of treatment, and in the 3 female patients, who had rather extensive pelvic inflammatory conditions, between 15 and 120 hours. The length of treatment for the men varied from 2 to 3 days. Two of the women were treated for 3 and 5 days, respectively. The necessity of extending the treatment for 6 days for the other woman was found to be due to loss of potency of the penicillin. From these findings, it appears that the results in the treatment of women with pelvic infections due to gonorrhea are comparable to those reported for men. Cases of 2 of the women treated are reported in detail.

The penicillin was administered by means of the intravenous drip method which has previously been described in the literature. For the male patients in

this series the dosage ranged from 65,000 to 110,000 Oxford units, and for the female patients from 113,000 to 162,000 Oxford units.

Because of the ease of administration, the small amounts of penicillin required, the lack of discomfort to the patient, and the absence of any untoward reactions, it seems reasonable to assume that penicillin therapy will replace the methods now used in the treatment of sulfonamide resistant gonorrhea. Since this report was made, Mahoney and his coworkers have reported success in 74 out of 75 male cases of sulfonamide resistant gonorrhea through the use of penicillin treatment.

**The treatment of gonorrheal ophthalmia by diathermy in conjunction with sulfonamides: Report of 3 cases.** Frank P. Smart, Charles A. Young and Kenneth Phillips. U. S. Nav. M. Bull., Washington, 41: 1727-1730, Nov. 1943.

The first case was seen by Smart in 1927. A nurse, while on duty, received a splash in the eye from a bed pan. In about 36 hours gonorrheal ophthalmia developed. All indications were that the eye would be lost and the patient was given long-wave diathermy locally to the eye for 30 minutes at the highest intensity tolerable. This was repeated every 8 hours for three sessions. The patient completely recovered; vision was altered only to the extent of that caused by a small healed ulcer.

The second case was that of a seaman admitted on Feb. 12, 1943, with gonorrheal ophthalmia caused from infected hands. He was given 15 gr. sulfathiazole every 3 hours during the 24-hour period, and short-wave electromagnetic induction to the eye for 30 minutes. Within 6 hours improvement was seen. The short-wave applications were continued for 30 minutes each 24 hours for 7 treatments. Spreads were negative for gonococci after 48 hours. The sulfathiazole was stopped after the third day. Recovery was complete without alteration of vision 12 days after admission.

The third case was admitted to the hospital on Apr. 8, 1943, with acute gon-

orrheal ophthalmia. The patient was given 30 minutes' application to the eye with ultra-short-wave spaced condenser plates, followed by 15 gr. sulfathiazole every 3 hours during the 24-hour period and frequent normal saline irrigations. Improvement was noted after 6 hours. The diathermy was not repeated; sulfathiazole was continued for 48 hours, then reduced to 15 gr. three times a day, for 2 days, and then stopped. Spreads became negative in 48 hours following the beginning of treatment. Recovery was complete with no alteration of vision 18 days after admission.

Since these cases were reported, the authors have treated 2 additional cases with equally good results.

From his experience over the past years, Phillips contends that temperature alone is not the sole factor in curing these infections; numerous cases have been cured with temperatures lower than the thermal death point of the organism. Other bodily immune factors must be stimulated.

Both the short-wave, ranging from 16 to 30 meters, and the ultra-short-wave from 6 to 10 meters, wave lengths were used. The application can be given with safety for 30 minutes every 3 hours during the 24-hour day.

The authors conclude that the value of diathermy for gonorrheal ophthalmia has been established since symptomatic and clinical improvement resulted before adequate amounts of sulfonamides had been received. The combination of these two treatments is recommended for speed and completeness of recovery.

**Treatment of acute gonorrhea by a mass unit (10 grams) dosage of sulphapyridine.** W. H. Dickinson Priest. J. Roy. Army M. Corps, London, 81: 139-141, Sept. 1943.

An analysis is made of 485 cases of acute gonorrhea treated at a military hospital in England. Ten grams of sulphapyridine were given each patient immediately upon his admission to the hospital. The tablets were crushed to powder and given in half a pint of milk.



The patient was confined to his bed for 24 hours and placed on a liquid diet with a large amount of water or barley water. Nausea without vomiting often occurred with this dose.

In 86 patients (17.7 percent) an extra maintenance dose of 4 gm. sulfapyridine was given during the subsequent 48 hours, but this was discontinued as the patient did not need it and the stay in the hospital seemed to be longer. In 379 patients (78 percent) no further routine treatment was necessary and their average stay in the hospital was 9.4 days. In 106 patients (21.8 percent) additional routine courses of sulfapyridine were necessary and their average hospital stay was 23.7 days. The total average stay in the hospital was 16.6 days. There were 7 known relapses. Irrigations when given were anterior or posterior as indicated, and were of a solution of potassium permanganate 1:8,000 daily or twice daily. No toxic results were seen. Forty-three percent of the cases were followed to their final tests of cure.

It was possible to trace only 31 percent of the infecting contacts. Inquiry disclosed that 6 percent of the infections were due to admitted professional prostitution, 2.1 percent to members of the Women's Services, 15 percent to marital infection, 62 percent to "amateur" encounters or liaisons, and 15 percent denied exposure.

**Disorders and lesions of the male urethra. Office procedures.** Edgar G. Ballenger, Harold P. McDonald and Reese C. Coleman. J. A. M. A., Chicago, 123: 599-603, Nov. 6, 1943.

While many urologists do not treat venereal diseases, the treatment of gonorrhea is an office procedure which should have careful consideration by those who do treat it. In cases of acute gonorrhea, when the discharge has been present for less than 48 hours, the combined use of sulfathiazole orally and a 5 percent solution of mild protein silver sealed in the anterior urethra once a day for 4 days has brought a high percentage of prompt cures. The sulfathiazole is given in doses

of 1.5 gm. 4 times a day for 2 days, then 1 gm. 4 times daily for 2 more days. After urination 1.5 cc. of freshly prepared 5 percent solution of mild protein silver is injected into the urethral meatus and held there by means of a clamp. An application of collodion is made and when the collodion has dried the clamp is removed and a condom put on for 4 hours if possible.

For cases of acute gonorrhea in which the discharge has been present for more than 48 hours, the chances are about 80 to 90 percent that a cure may be effected within 2 weeks or less with sulfathiazole. This implies that the patient can tolerate the sulfonamide in doses of 1 gm. 3 or 4 times a day. In chronic or recurrent gonorrhea probably the commonest causes of failure to obtain satisfactory cures with sulfathiazole are stopping the drug too soon and a pocketed infection in the glands of Littre or at urethral strictures.

Ambulatory patients who are taking sulfonamide drugs should be warned of the possibility of nausea and dizziness; drug fever is occasionally seen, and skin rashes are not uncommon.

**Sulfanilamide sensitization: Report of renal and hepatic damage in a fatal case.** C. Frederic Roche and Donald G. Stannus. J. Florida M. A., Jacksonville, 30: 196-199, Nov. 1943.

A 35-year-old woman was admitted to St. Francis Hospital, Miami, on Dec. 7, 1939, suffering from nausea, vomiting, severe jaundice and pain in the muscles of both legs and the left elbow. She had come to Miami to recuperate on her physician's advice following a gonococcal infection, and had had surgery for an "abscess on the vagina" since her arrival. She was given sulfanilamide at that time. On admission to the hospital her temperature was 98°, but it rose to 103° F. the next day. The skin and conjunctivas were greatly jaundiced. Because of a decrease in red blood cells and great increase in edema she was given 500 cc. of citrated blood. The jaundice increased, and on December 15 the icterus index was 98 and it remained at this level throughout the



illness. The white blood cell count increased from 19,000 to 50,000. In spite of repeated transfusions and intravenous administration of saline solution and a 50 percent solution of hypertonic glucose, death occurred 20 days after admission. Autopsy findings were jaundice, purpuric spots, generalized edema, and pathologic changes in the brain, heart, spleen, kidneys, bladder, and liver.

In the authors' case, apparently catarrhal jaundice played an important part in the subsequent toxic hepatitis and nephrosis due to sulfanilamide. Since Weil's disease was ruled out by laboratory procedures, this case was diagnosed as extensive necrosis of the liver with associated nephrosis, transient neuritis, purpura and death caused by sulfanilamide. The authors stress the importance of hepatic and renal function tests before chemotherapy.

**Agranulocytosis associated with sulfadiazine therapy.** Edmund B. Flink and Theodor E. Bratrud. *Minnesota Med.*, St. Paul, 26: 898-899, Oct. 1943.

The authors report a case which they consider as the only instance of agranulocytosis with a fatal outcome which has occurred at the University of Minnesota Hospitals following the use of any of the sulfanamides.

The patient, a woman aged 28, was in the hospital for 5 days following Sept. 29, 1942. The hemoglobin concentration was 4.4 gm. percent, the erythrocytes 2,789,000 per cu. mm. and leukocytes 4,850 on admission. Cultures of venous blood showed growth of *Streptococcus viridans*. She returned to the hospital 12 days later. She was given sulfadiazine intermittently, but the drug did not produce any clinical benefit. Her general condition improved following transfusions. She had a constant fever with an average daily temperature peak of 102° F. On November 4 her leukocyte count was 950 cells per cu. mm. with 42 percent neutrophils, 56 percent lymphocytes and 2 percent monocytes. Sulfadiazine was discontinued immediately. The next day agranulocytosis

existed, and continued until death 4 days later. During this time, the total leukocyte count ranged from 2,300 to 500 per cu. mm.

The anatomic diagnosis after a limited autopsy included acute agranulocytosis, patent interventricular septal defect, and subacute bacterial endocarditis.

The agranulocytosis developed 20 days after instituting therapy with sulfadiazine, of which a total of 54 gm. was given. The sulfadiazine appeared to have been the cause of the agranulocytosis because no other drugs were administered immediately prior to the onset.

**Studies on the side-effects of sulfaethylthiodiazol.** (Untersuchungen über die Nebenwirkungen von Sulfaäthylthiodiazol.) H. Sapinski. *Deutsches Arch. f. klin. Med.*, Berlin, 191: 70-86, May 18, 1943.

The side-effects of sulfanilamido-ethylthiodiazole (globucid) were studied clinically. It was found that this drug has no effect on the peripheral blood picture or on bone marrow function. The quantitative and qualitative composition of the normal elements of the blood, and the bleeding and coagulation time remained normal, even after high dosage and long continued administration of the drug. With its use, hemolytic anemia or agranulocytosis need not be feared. Blood protein determinations showed that globucid apparently does not have a nonspecific irritative effect. Studies of liver, kidney, and intestinal function showed that this drug had no ill effect on these organs. Hepatitis, nephritis, and anemias are not considered to be contradictions to globucid therapy.

Occasionally it produces increased fasting hydrochloric acid values of the gastric juice. Studies with pyrifur (for the production of fever) showed that globucid (like cibazol) has no central fever-reducing effect. However, the leukocytosis produced by pyrifur injections is somewhat inhibited by globucid. No decrease in the fasting blood sugar level and no influence on the sugar tolerance blood sugar curve were observed.

**Vitamin E (wheat germ oil) in the treatment of interstitial keratitis.** Simon Stone. Arch. Ophth., Chicago, 30: 467-475, Oct. 1943.

Since March 1940 the author has treated 10 patients with advanced interstitial keratitis with vitamin E (wheat oil and wheat germ oil concentrate). All had received ample antisyphilitic therapy previously. Because of associated involvement of the central nervous system 4 had received artificial fever therapy a number of months earlier, but without its markedly affecting the course of the keratitis. Two patients were given artificial fever treatments shortly after therapy with vitamin E was begun.

Vitamin E was mainly effective in hastening absorption of superficial and deep corneal exudates; it helped to relieve the associated photophobia and reduce excessive corneal vascularization and circumcorneal congestion. In case of long standing involvement with extensive opacities and corneal scarring, its administration for a period of months has produced a gradual and continuous clearing of the cornea with a return of normal vision. In one case complete clearing of the cornea occurred with a return of normal vision. In one case complete clearing of the cornea occurred after 18 months of vitamin therapy although only perception of light was present in one eye and perception of fingers in the other when therapy was begun. Absorption of corneal exudates and return of normal vision took place in another case after 4 weeks of vitamin therapy alone.

Riboflavin when administered alone or in combination with vitamin E was effective primarily in relieving some of the photophobia and reducing the extent of circumcorneal injection and capillary proliferation. It appeared to have no effect, however, on the rate of absorption of corneal opacities and scars.

The author believes that vitamin E combined with vitamin B complex is a most valuable adjunct in the treatment of interstitial keratitis. If the patient has received ample treatment in the past, antisyphilitic therapy is apparently not

needed to produce complete disappearance of the visual symptoms and corneal opacities of interstitial keratitis. Artificial fever therapy is of value mainly in preventing relapses and in producing more rapid amelioration of acute symptoms. It has little effect when administered alone on the rate of absorption of corneal opacities of long standing.

**The intensive treatment of gonorrhea and syphilis. Organization, objectives, activities and accomplishments of the Chicago Intensive Treatment Center: Preliminary report.** Herman N. Bundesen, Theodore J. Bauer and H. Worley Kendell. J. A. M. A., Chicago, 123: 816-820, Nov. 27, 1943.

The authors report on the patients treated for syphilis and gonorrhea at the Chicago Intensive Treatment Center between Nov. 29, 1942 and Oct. 8, 1943. This is a preliminary report; a longer period of observation is necessary before deductions can be made regarding the actual value of the systems of treatment being employed.

Three methods of intensive treatment for early syphilis are employed: (1) Fever-chemotherapy, in which each patient receives 8 hours of fever maintained at 106° F. (rectal) by means of the hypertherm plus mapharsen and bismuth therapy; (2) intensive chemotherapy, in which at present the patient receives 80 mg. of mapharsen twice daily for 7 days (regardless of weight) by the multiple syringe method, and 150 mg. of elemental bismuth (2 cc. of bismuth subsalicylate in oil) intramuscularly in one dose every second day for 4 doses; (3) long term intensive chemotherapy, by which the patients are given 1 mg. of mapharsen per kilogram of body weight, administered by the multiple syringe method 3 times weekly for 8 weeks, combined with 75 mg. of elemental bismuth (1 cc. of bismuth subsalicylate in oil) administered intramuscularly in one dose twice weekly for 16 doses.

Patients remained in the center until active lesions of the skin and mucous membrane were healed. The average



stay was 7 days in the fever-chemotherapy section and 14 days in the intensive chemotherapy section.

An advisory board was appointed to determine the routine and dosages used in intensive treatments. Specialists made physical examinations and laboratory study of each candidate for treatment. After diagnosis was established the admitting clerk assigned the patients to the form of treatment, in a ratio of two to the fever-chemotherapy section and one to the intensive chemotherapy section.

Following the first death in fever-chemotherapy, the dose of mapharsen was reduced from 120 to 60 mg. in a series of 241 consecutive cases. In the present series of 488 patients the dose was raised to 1.76 mg. per kilogram of body weight.

A series of 390 patients was treated with intensive chemotherapy, 172 receiving 1,200 mg. of mapharsen within 10 days. This group was observed for 7 months. Ten had mucocutaneous relapses. The method was discontinued since reactions severe enough to stop treatment were encountered in 11.9 percent of the patients treated. A modification was then adopted whereby all the mapharsen was given within 7 days, with bismuth being given in addition. Under this regimen 208 patients were treated, but the time is too short to allow conclusions as to results.

Those patients who were rejected for fever-chemotherapy and for intensive chemotherapy were treated by the long term chemotherapy. Of the 81 patients treated by this system, 52 have become serologically negative and 1 had serologic relapse.

A detailed report of the results of the treatment of a total of 1,786 patients admitted for the treatment of gonorrhea during the period being considered will be made when statistics are available.

**A new approach to the treatment of early syphilis by intensive therapy.** T. R. Lloyd Jones and F. Gordon Maitland. *Brit. M. J.*, London, No. 4318: 448-451, Oct. 9, 1943.

The authors present a new conception of early syphilis based on the results of

the quantitative Kolmer-Wassermann test performed daily on a series of 100 patients undergoing intensive therapy. In order to provide a fair and reliable index of the intensity of the individual patient's infection, early syphilis was divided into three distinct groups—the early primary, the middle primary, and the late primary types—the grouping being based on the type of serologic response, which is described in detail. In the early primary and middle primary groups the abortive treatment is required, while in the late primary group a curative dose is necessary. The duration of treatment would be 15, 20, and 30 days, respectively, dosages ranging from 600 to 900 mg., 900 to 1,200 mg., and 1,200 to 1,800 mg. mapharsen (mapharside), respectively, depending on body weight. A fixed, predetermined dosage is not recommended. It is believed that the longer time-factor would lower the toxic effects.

One case of agranulocytosis was seen in the entire series of cases. This developed after a dosage of 1,130 mg. in a late primary case. Recovery was complete following 110 cc. pentnucleotide. There were 11 cases of jaundice seen.

There were 3 cases of relapse and 3 of reinfection.

A detailed description of the laboratory procedure is given.

**Arsphenamine tolerance during menstruation.** (Über die Salvarsanverträglichkeit bei Menstruation.) A. Beck. *Deutsche med. Wehnschr.*, Leipzig, 69: 488-489, June 25, 1943.

In a number of cases untoward reactions to arsphenamine injection were observed to occur during the menstrual period. Twelve cases are reported, all but 3 of which were cases of primary or secondary syphilis. The reactions occurred following the administration of arsphenamine or neoarsphenamine in moderate dosage during the menstrual period and included "spirochetal-fever" in 3, skin eruptions in 7 (3 of which were severe), angioneurotic edema in 1, and encephalitis in 1 of the patients. None of the reactions were fatal. In cases in which



severe skin eruptions occurred, the menstrual flow became scant or stopped altogether. In several cases amenorrhea was observed following the reaction.

The explanation given for these reactions is that during menstruation the threshold of tolerance of arsphenamine is lowered. The author advises that arsenical injections should not be given immediately before or during the menstrual period.

**Toxic effects of arsenical compounds as administered in the United States Navy in 1942 with special reference to arsenical dermatitis.** Thomas J. Carter, Wesley M. Chambers and Laura T. Anderson. U. S. Nav. M. Bull., Washington, 41: 1777-1785, Nov. 1943.

The following number of doses of arsenicals were administered by the U. S. Navy during the year 1942: Acetarson, 42; bismarsen, 665; mapharsen, 109,095; neoarsphenamine, 9,756; silver arsphenamine, 5; sulfarsphenamine, 69; tryparsamide, 2,474; a total of 122,106. There were 27 reactions from mapharsen, 7 from neoarsphenamine, and 1 fatality from silver arsphenamine. This was a total reaction rate of 1 per 3,489 doses and a death rate of 1 per 122,106 doses, the reaction rate for mapharsen being 1 per 4,041 and neoarsphenamine 1 per 1,394 doses. During the 18-year period, 1925-42, there was a total of 1,914,519 doses administered, with a reaction rate of 1 per 1,660 and a death rate of 1 per 36,123 doses.

In 1942 dermatitis in some form occurred in 17 cases, or 49 percent of the total reactions, as compared with 45 percent for 1941. In 6 instances the lesion was erythematous, in 3 exfoliative, in 4 macular, in 3 maculopapular, and in 1 urticarial. In 7 cases the reactions were mild and occurred 1 each after the third, fourth, fifth, seventh, ninth, twelfth, and eightieth injections. The interval between the injection and appearance of symptoms varied from 1 hour to 2 days. The length of time required for complete recovery varied from 14 hours to 7 days.

In 10 cases the reactions were severe; 1 occurred after the first injection, 3 after the third, 2 after the fourth, and 1 each after the fifth, eighteenth, nineteenth, and forty-fifth. The interval between the injection and appearance of symptoms in these severe cases varied from 1 hour to 25 days. One reaction was believed to have been caused by an accumulative poisoning due to repeated injections and not to any one injection. The length of time required for recovery varied from 4 to 47 days. The ratio of arsenical dermatitis cases was 1 to 7,183 doses. Premonitory signs occurred in 5 instances.

**Arsenical toxæmia: A selection of cases.** H. J. Bell and A. E. Wilkinson. J. Roy. Army M. Corps, London, 81: 119-127, Sept. 1943.

In the past few months the authors have seen 30 cases of arsenical toxemia in soldiers undergoing antisyphilitic treatment in the Middle East. The drugs used were neosalvarsan, novostab and sulfo-stab. The most severe case of toxemia was in a man who had been receiving antisyphilitic treatment for 7 months and had not previously shown any signs of arsenic intolerance. This patient developed toxic purpura with massive hemorrhage and profuse hematuria, complicated by subretinal hemorrhages in the macular regions of both eyes. He was given three-fourths pint of citrated blood and one-half pint of glucose saline by slow intravenous drip, and except for some temporary visual disturbance due to clots in the macula which eventually were resolved, recovery was uneventful.

In the second case severe jaundice developed, possibly due to subacute necrosis of the liver, following the second injection of arsenic. Insulin and glucose improved the patient's condition. In the third case, sudden edema of the face and throat occurred after the second injection of neoarsphenamine, which disappeared rapidly under treatment with glucose, insulin, and ascorbic acid.

In the fourth case, within 2 hours of an injection of arsenic, acute toxemia suddenly developed which responded to treatment with insulin. The fifth case, apparently a healthy man, developed serous apoplexy which proved fatal. He had been given a course of sulfonamide (30 gm.) by mouth concurrently with his early arsenical injections. The autopsy findings were intense congestion of the blood vessels on the surface of the brain, widespread but minute petechial hemorrhages in the brain substance itself, and histologic picture of acute toxemia in the liver.

Nine cases of arsenical dermatitis were seen in the clinic, all of which recovered. Glucose, alkalis, ascorbic acid, and sulfur orally and injections of sodium thiosulfate were used in the treatment of these cases, with the exception of one. In this case, following the initial treatment with fluids, glucose, ascorbic acid, and alkalis, 10 units of insulin were injected, followed 5 hours later by 5 units. The following day the same dosage of insulin was given at a 7½-hour interval. On the third day, 5 units of insulin were given, followed 10½ hours later by another 5 units. On the fourth day, the last dose of 10 units of insulin was given. Glucose was given daily. At the end of the fourth day, the capillary resistance test was negative and the patient was discharged fit for service. This patient was called back to the clinic 1 month later for a "patch test." Within 2 hours after application of arsenic to the skin, he experienced a burning sensation. Examination of the skin 24 hours later, when the patch was removed, showed a swollen, hot and erythematous area, covered with small papules and vesicles. This case gives support to the opinion that arsenical dermatitis is caused by the skin becoming sensitized to the drug itself.

The authors report these cases to show that insulin may be used with great advantage in the treatment of the later toxemias of arsenic, and that the liver is of primary importance.

**Examination and treatment of native women for venereal disease.** R. G. Gibson and R. Park. *East African M. J., Nairobi*, 20: 180-185, June 1943.

In spite of their intensive efforts to control the venereal diseases among the African troops, the medical officers realized in the fall of 1942 that these diseases were depleting the troop personnel to an alarming degree. It became obvious that the main source of the infection was the women of the location. The Kenya police offered to cooperate, and on Oct. 17, 1942, they sent in 15 women to be examined. It was decided to do cervical and urethral spreads on all women, and only those found to be negative would have a Kahn test. Of the first 97 women examined, only 14 were found to be free of both gonorrhea and syphilis; 56.6 percent were positive for syphilis and 54.5 percent for gonorrhea.

A scheme for examination and treatment, with the minimum of discomfort and disturbance to the medical officers and to the patients, was worked out. In solving the problems of treatment, it was necessary to consider the supplies of M. & B. 693 (sulfapyridine) and of N. A. B. (nearsphenamine) as well as the best method of administration for the native women. For gonorrhea, it was decided to give 3 intramuscular injections of a suspension of 1 gm. of sulfapyridine in 1 cc. of sterile water. This method, combined with 2 minims of T. A. B. intravenously, was resulting in the cure of troops in an average of 6 days, with only a 6 percent recurrence. For syphilis, nearsphenamine and bismuth in the "concurrent-intermittent" method was decided upon.

After more women were sent in, it was found that 87 percent of 192 women examined were infected; 95 women out of 169 examined for gonorrhea were positive and 87 out of 139 Kahn tests were positive. Twenty-five women were free from both diseases. Of the 90 women who started treatment for gonorrhea, 88 completed it, and of the 82 who reported for examination after treatment 70.9 percent had neg-



ative spreads. About half of the women seemed grateful for the treatment. There were a few reactions from the antisyphilitic treatment, which it was feared would keep the women from being treated.

The nurse who arrived from England took over all the examinations and is gradually supervising the treatment, which lessens the work of the medical officers. She has found that the headman's house and a school are being used as brothels, and that Moslems are accepting sums of money to claim women as their legal wives.

At the time of writing, 362 women have been examined, 228 have been treated for gonorrhea and 206 for syphilis. Of 182 women recently reexamined for gonorrhea, 22 percent were found to have positive spreads. It is now planned to examine all the women monthly.

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## **PATHOLOGY**

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**Diversified pathological processes in the aorta.** Solomon F. Hoge. M. Bull. Vet. Admin., Washington, 20: 217-219, Oct. 1943.

A 73-year-old male patient was seen at the Veterans' Administration Facility, Wadsworth, Kansas, in April 1938. He complained of persistent pain in the left upper chest and abdomen, without exacerbations or radiations. He had contracted syphilis during the Spanish-American War, but could give no information regarding treatment for this condition. His serologic reaction was strongly positive and his blood pressure 200/120. At this time a diagnosis of atherosclerosis, hypertension, senility, arthritis, and chronic gastritis was made. He was next seen in August 1941 at another Facility. At this time the former diagnosis was confirmed with the addition of syphilitic meningoencephalitis and fusiform aneurysm of the descending aortic arch. Examination showed no enlargement of the first part of the arch of the aorta. The lungs were clear. The electrocar-

diogram showed left axis deviation suggestive of hypertension or aortic valvular disease. The blood pressure was 120/80. He improved under antisyphilitic treatment and was sent back to the Facility at Wadsworth for domiciliary care. His condition remained satisfactory until Mar. 21, 1943 when he complained of dyspnea and cough. His condition steadily grew worse until his death Apr. 22, 1943.

Upon post-mortem examination the heart was negative for gross change. The first part of the aortic arch presented a fusiform dilatation, with tenting of the wall. There was a definite elongated bulging, beginning on the anterior median surface of the descending arch and continuing through the crux of the diaphragm. Further dissection showed the stoma of the innominate, common carotid and the subclavian arteries were of average caliber. The aortic ring exhibited no gross pathologic change. Four centimeters beyond the aortic ring was a free edge or a sheet of tissue made up of intima and part of the media, with a smooth rounded margin extending around the wall of the vessel. The distal side of the trough was fibrotic and fused into an annular septum of tissue with an aperture that admitted the first phalanx of the index finger. The distal side of this thickened, smooth-margined septum fused into and was continuous with the intima of the transverse aortic arch. There was little or no expansion of this septal aperture, and it was fairly fixed as to its movements with the passing column of blood. The findings indicated a completed aneurysm of the intima and part of the media, with loose shelving of the proximal fringe, a stripping-up and rolling of the distal fringe into the fibrotic septum.

The author feels that this case is of interest as it shows the extreme changes which the aorta may undergo before causing death. It could not be determined whether the partial rupture bore a definite chronologic relationship to the dissecting aneurysm or rupture into the main channel of the abdominal aorta.



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## LABORATORY RESEARCH

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**Sterility test for penicillin.** C. A. Lawrence. *Science*, Lancaster, 98: 413-414. Nov. 5, 1943.

A method of testing penicillin for sterility required some chemical or physical agent which would inactivate the substance completely and have no antibacterial effects on possible contaminating organisms in the product. Of the various agents tested, two enzyme preparations, Taka-diastase and clarase, seemed to meet these requirements. These enzymes were found to inactivate the antibacterial effects of penicillin in 2 hours or less when incubated in the presence of the agent in a water bath at 40° C. and tested by the Oxford cup-plate method. Taka-diastase was effective under these conditions at pH 6.0 and 8.0 but not in buffer solution of pH 4.0. Clarase neutralized penicillin activity completely at all the pH ranges given. Further studies showed that Taka-diastase was effective in this test in dilutions of 1:200, while clarase gave a similar action in a final dilution of 1:4,000.

A study of the effects of the enzyme system against the agent in the presence of a fluid medium by the use of clarase was carried out in the following manner: A 1 percent stock solution of clarase was prepared in buffer solution of pH 7.0 and sterilized by Berkefeld filtration. Samples of sodium penicillin powder, as received in the sterility control laboratory, were inoculated with dry cultures of *Clostridium tetani*, *C. septique*, *Bacillus subtilis*, *Eberthella typhi*, *Escherichia coli* and *Staphylococcus aureus*. To the dry contaminated powders were added 2 cc. of the prepared clarase solution. The enzyme penicillin solutions or suspensions were transferred immediately to several tubes of Brewers' fluid thioglycollate medium. The contents of the tubes were mixed thoroughly by swirling and placed at 37° C. to incubate. A luxuriant growth

of the inoculated test organisms was had in all tubes at the end of 48 hours. Control tubes containing gram-positive organisms and penicillin, but without enzyme, failed to show evidence of visible growth at the end of 7 days' incubation. However, many of the tubes containing gram-negative organisms and penicillin without enzyme showed some growth after several days, which is to be expected on the basis of known resistance of most gram-negative bacteria to the antibacterial agent.

From the experimental studies, the following method for routine sterility tests on penicillin powder is proposed: A stock of 1 percent sterile solution of clarase in phosphate buffer, pH 7.0, is distributed in 2 cc. amounts in sterile cotton plugged test tubes or in ampules which may be sealed. The sterile enzyme solution will retain its antipenicillin activity for at least 2 months if stored in a refrigerator. The contents of an ampule of penicillin are dissolved or suspended in 2 cc. of prepared clarase solution and transferred immediately to tubes of Brewers' fluid thioglycollate medium. The inoculated tubes are placed at 37° C. and examined for possible bacterial contamination for 7 days. An additional 7 days' incubation should be allowed for detection of possible mold contamination.

**Microbiological aspects of penicillin. II. Turbidimetric studies on penicillin inhibition.** Jackson W. Foster and Bernard L. Wilker. *J. Bact.*, Baltimore, 46: 377-389, Oct. 1943.

Contrary to results with the plate method, the authors have found that by turbidimetric measurements the same amount of penicillin is required to effect a 50 percent growth inhibition of *Staphylococcus aureus* H in nutrient broth at pH 5.0, 5.5, 6.0, 6.5, 7.0, 7.5, and 8.0. The presence of glucose and other sugars in the medium causes irregular breaks in the inhibition curves. This is apparently due to an alteration or partial inactivation of penicillin which occurs when sterile penicillin and glucose broth solutions are allowed to stand before inoculation. The effect is not obtained in

the absence of glucose. It also takes place during the regular 16-hour incubation period. The inactivation is less at 2° C. than at 37° C. and could be found only at certain concentration levels of penicillin. Penicillin inhibition of *S. aureus* is due to logarithmic prolongation of generation time and not to selection of resistant cells. The stability of penicillin is best between 4.8 and 7.9. It is inactivated very rapidly beyond these extremes.

**Notes on modification of the Werner method for the determination of sulfonamides.** S. W. Lee and N. B. Hannay. *J. Am. Pharm. A. (Scient. Ed.)*, Washington, 32: 307-308, Nov. 1943.

Modifications of the Werner method for the determination of sulfonamides were studied and are reported in detail.

An adaptation of the method of Churg and Lehr gave accurate results in the determination of free sulfonamides when blank readings (before medication or addition of drug) were taken. Blood samples which did not give appreciable readings with the Bratton and Marshall method, gave levels up to 2 mg. per 100 cc. with this procedure. The blank blood readings were additive and the recovery of added sulfathiazole was high. Blood taken from 6 persons who had not received sulfonamide was used. Blanks were run on the samples by 2 methods and sulfathiazole was added at 2 levels for the purpose of studying recovery by this method. It was found impossible to obtain accurate results on total sulfonamides, using either the method of Churg and Lehr or the adaptation of this method.

**Observations on the urinary excretion of sulfadiazine.** Osler L. Peterson, Robert A. Goodwin, Jr. and Maxwell Finland. *J. Clin. Investigation*, Lancaster, 22: 659-672, Sept. 1943.

The authors present the results of attempts by various procedures to induce diuresis of the drug and of urine in persons receiving sulfadiazine in ordinary therapeutic doses. The following procedures were investigated in men who, during convalescence from mild complaints,

were kept in the hospital particularly for this purpose: (1) Intravenous injection of 1,500 ml. of a 5 percent solution of glucose in distilled water; (2) intravenous injections of 1,500 ml. of 0.85 percent sodium chloride solution in water; (3) ingestion of 1,500 ml. or more of cold tap water; (4) intravenous injection of 100 ml. of 50 percent glucose solution; (5) ingestion of 15 to 25 gm. of sodium bicarbonate with a small amount of water, and (6) a few observations on the effect of urea and ammonium chloride. Studies were made on the fate of single doses of drug in the same subject during periods of high or low fluid intake. The results of all these procedures are discussed at length and accompanied by graphs.

The authors summarize their conclusions from this study as follows: The greatest and most prolonged increase in excretion of sulfadiazine resulted from the administration of alkali (sodium bicarbonate) in amounts sufficient to insure a highly alkaline urine. A decrease in the concentration of the drug in the urine was obtained most rapidly by the intravenous injection of a large volume of 5 to 10 percent glucose solution in distilled water. The ingestion of water in large amounts produced a similar result somewhat less rapidly. The intravenous infusion of physiologic saline gave a less marked reduction in the concentration of drug in the urine and the effect was more delayed. Only the first of these 3 procedures was accompanied by a large increase in drug output.

Care should be taken to insure proper hydration of a patient before undertaking the intravenous injection of large amounts of sulfadiazine.

**The successful treatment of granulocytopenia and leukopenia in rats with crystalline folic acid.** Floyd S. Daft and W. H. Sebrell. *Pub. Health Rep.*, Washington, 58: 1542-1545, Oct. 15, 1943.

The authors tabulate the results of their tests of xanthopterin and of crystalline folic acid solutions in the treatment of granulocytopenia and leukopenia in animals on a purified diet.



From the results it was seen that doses of 20 or 40 micrograms of xanthopterin a day for 4 days did not correct the blood dyscrasias. The average total leukocyte count at the beginning of the test was 2,750 per cu. mm., with 2 percent granulocytes. After 4 days of treatment with xanthopterin, the average total leukocyte count was 2,450 per cu. mm., with 1 percent granulocytes. The results showed, however, that the three solutions of crystalline folic acid showed definite activity in the amounts tested. For example, the administration of 0.2 cc. solution 38453 (calculated as containing 20 micrograms) daily for 4 days gave an average increase in total leukocytes from 2,700 per cu. mm. to 14,400 per cu. mm. and an average increase in the percentage of granulocytes from 1 to 39 percent.

The effect of solutions of crystalline folic acid on anemia was tested in 9 rats. Seven of these animals recovered during the 10-day testing period. The average hematocrit increased from 29.8 to 42.1 volumes percent, the average erythrocyte count from 5.1 to 6.9 millions per cu. mm., and the average hemoglobin from 9.7 to 12.8 gm. percent. In 2 animals the values declined. From these results, the authors think it probable that crystalline folic acid also has antianemia activity.

**An agglutination test for the serological diagnosis of syphilis.** F. M. Berger. *J. Path. & Bact.*, London, 55: 363-371, July 1943.

Since only about 80 percent of syphilitic serums give a positive reaction with the numerous complement fixation and flocculation tests for syphilis, the author feels that there is need for a simple and rapid preliminary test which would give a positive reaction with all serums containing the reacting substance without yielding nonspecific results in an unduly high percentage of cases. After such a screen test was used, all negative serums could be reported at once.

He describes an agglutination reaction, in which suspensions of collodion particles treated with diluted Kahn antigen and subsequently washed were used as

antigen. The sensitized collodion particles were agglutinated by serums from patients who had syphilis. The preparation of the suspension of collodion particles and their sensitization are described in detail. The technics for qualitative and quantitative tests also are discussed.

A series of 2,452 serums was examined by the Wassermann, Kahn and agglutination tests. Of the 562 known syphilitic serums all were positive by the agglutination test as compared with 66 and 67 percent positive by the Kahn and Wassermann tests, respectively. The percentage of nonspecific reactions with the agglutination test was no greater than with the other widely used tests of lower sensitivity.

It was possible to standardize the sensitivity of the agglutination test by controlling the agglutinability of the sensitized particles. The test possessed an inherent sensitivity equal to that of the complement fixation test. Its actual sensitivity was greater still, as factors causing false negative reactions in the Wassermann test were without influence on the agglutination test. The qualitative agglutination test appeared to be well suited for use as a very sensitive presumptive test. By means of the quantitative test the titer of the reacting substance in serum could readily be determined.

**An inhibition phenomenon in precipitation tests for the serodiagnosis of syphilis.** Rachel Brown. *J. Lab. & Clin. Med.*, St. Louis, 28: 1758-1760, Nov. 1943.

The precipitation test for the serodiagnosis of syphilis is evidently subject to a phenomenon of inhibition in which the reaction between serum and antigen becomes manifest only under certain conditions. This inhibition appears to be distinct from the prozone phenomenon although the two may occur together.

The author feels that this phenomenon is of sufficient importance to require further investigation and careful consideration in the standardization of the tech-



nical procedure of precipitation to avoid the possibility of a false interpretation of the results.

**Chemotherapy of experimental lymphogranuloma venereum in mice.** Fritz T. Callomon and Herman Brown. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, 27: 590-600, Sept. 1943.

Three strains of lymphogranuloma venereum virus were used in inoculation of 171 white mice, of which 122 were treated with various sulfonamides and 49 served as untreated controls. Sulfathiazole, sulfapyridine, sulfanilamide, sulfadiazine, and neoprontosil were used in treatment of the different groups, and the results of the treatment determined.

Sulfathiazole proved most effective in chemotherapy of lymphogranuloma venereum infection, sulfapyridine and sulfadiazine were next, while the effect of sulfanilamide and neoprontosil was considerably less. These results seem to agree with the experience of clinicians in the treatment of human infection.

The amounts of sulfonamide penetrating the brains as the result of treatment were variable and appeared to be largely independent of dosage; factors involving the general health of the mice seemed to be of more importance.

It was found by reinoculation study that treated survivors remained carriers, although they had been apparently cured by sulfonamides. Some of the treated survivors, although they were protected by the sulfonamides after the initial inoculation, showed positive results after reinoculation, with some deaths. Some of the untreated survivors who were without any apparent symptom after the initial inoculation, showed positive results after reinoculation, with frequent deaths.

**Yolk sac complement fixation antigen for use in psittacosis-lymphogranuloma venereum group of diseases.** Joseph E. Smadel, Kenneth Wertman and Reginald L. Reagan. *Proc. Soc. Exper. Biol. & Med.*, Utica, 54: 70-74, Oct. 1943.

Observations of several groups of workers have suggested that the titers of se-

rum from patients with psittacosis and with lymphogranuloma venereum may differ somewhat when tested against homologous and heterologous antigens prepared from this group of viruses. The observations reported at this time extend those of others regarding the reactions of human convalescent serums with complement fixing antigens of psittacosis and lymphogranuloma.

The authors give in detail their method of preparation of psittacosis antigen from highly infectious material. It is said to be a comparatively simple and safe method. Three groups of convalescent serums were studied for their reactions with psittacosis and lymphogranuloma venereum antigens. The serologic data obtained indicate that the complement fixing antigen which is common in the viruses of the psittacosis-lymphogranuloma venereum group is present in about equal amounts in the authors' strains of psittacosis and lymphogranuloma venereum. Not only do antigens prepared from each agent react equally with equivalent amounts of antibody from the two diseases, but also comparable amounts of antibody are generally demonstrable in patients' serums when tested with either antigen. While slight differences are found in the antibody titers of certain serums when tested with the two antigens, these were neither sufficiently great nor consistent enough to enable one to differentiate between human psittacosis and lymphogranuloma venereum by this method.

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## **PUBLIC HEALTH ADMINISTRATION**

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**Syphilis patients in a marine hospital.** Gertrude G. Shay. *J. Social Hyg.*, New York, 29: 444-446, Oct. 1943.

The author, who is director of social hygiene at the Marine Hospital on Staten Island, N. Y., gave a talk at the Regional Conference on Social Hygiene, New York

City, on Feb. 3, 1943, in which she outlined the duties of a social worker in a service hospital.

The social worker sets aside regular hours for interviews, interpretation and education being carried on through interviews and group discussions. Patients are free to consult the office at any time. Literature in the patients' own language is prepared with special attention as to character-building material for the younger age group. Many patients are interested in making a scientific study of their disease. As soon as the patient accepts his diagnosis and adjusts himself to treatment, a constructive diversional program for the duration of hospitalization is undertaken. Motion pictures on health education are shown weekly. Other patients are given the opportunity to study any subject in which they may have especial interest. The use of the library is made available.

Before the patient leaves the hospital, the social worker reviews with him his plan for continuance of care and gives him information relative to clinic facilities available wherever he may plan to be.

Through interviews, the patient acquires an understanding of the disease and the meaning of treatment in freeing him of disease and reestablishing his security and confidence in the future. The success of the therapy and the control of the disease is determined by how the patient feels about having syphilis, what he has to do about it to get well, how he feels about getting well, how he feels about infecting others, and his intelligent understanding.

**The extent of the syphilis problem at the beginning of World War II.** R. A. Vonderlehr and Lida J. Usilton. New York State J. Med., New York, 43: 1825-1829, Oct. 1, 1943. Also: Am. J. Syph., Gonor. & Ven. Dis., St. Louis, 27: 686-696, Nov. 1943.

In 1938 the data presented on the prevalence of syphilis were obtained from attack rates calculated from the number of persons with early syphilis reporting

for the first time at authorized sources of treatment, serving approximately 5 percent of the population. The chance of persons acquiring syphilis by the age of 50 was calculated to be 1 in 10 if the attack rate in 1936-1937 prevailed. A second survey made in 1939-1941, using the same methods of calculations, showed that the chance of persons acquiring syphilis by the age of 50 had dropped to 1 in 15, a one-third decrease.

These chance rates, computed from treatment source surveys, were transposed into prevalence rates in order that they might be compared with the prevalence rates obtained through the routine blood testing of selectees and volunteers. From the tables which are given, it is seen that the estimates of prevalence based on attack rates are not inconsistent with the rates among the selectees. However, neither the prevalence based on the attack rates calculated for 1936-1937 nor that based on attack rates for 1939-1941 is strictly comparable to the prevalence among the selectees. In the first place, the prevalence among the selectees is based on the number of persons with positive blood tests and excludes all those who had at one time acquired syphilis but, from various causes, at the time of examination had negative blood tests. On the other hand, it was impossible to exclude blood reversals from the calculated prevalence. This, however, is in some part offset by the infections that do not come under treatment during the early stages of the disease. Furthermore, attack rates are not constant. In order to adjust in part for this fact, a new rate of prevalence was calculated, reflecting the attack rates of both surveys. Due to the reversal factor, these new rates are higher than the selectee prevalence rates, the difference becoming greater with age. When all adjustments are considered, as shown in the accompanying tables, the 1936-1937 calculations of the chance of acquiring syphilis may serve as a base line by which to measure the efficiency of subsequent syphilis control programs.



From this study, the authors report that in the 5-year period from 1936-1941, the chance of acquiring syphilis has dropped significantly. Furthermore, there is a reasonably accurate base against which to measure future attainments. They say that what the record will show from now on, no one can predict at present.

**Progress in wartime control of venereal diseases.** Felix J. Underwood. Mississippi Doctor, Booneville, 21: 181-182, Nov. 1943.

The most recent development in the control of the venereal diseases in Mississippi has been the establishment of three rapid treatment centers, where cases can be isolated during the period of infectivity, as well as treated under the accepted rapid methods of treatment for venereal disease. Several hundred private physicians are now cooperating on a part-time basis in Mississippi's extensive clinic program to combat the increasing number of cases of infectious syphilis and gonorrhea.

Since the centers began operation in April 1943, there have been 541 patients admitted to the centers at Meridian and Richton. The center at McLain will be ready within a short time. Of the patients admitted, 322 were white and 218 were Negro patients. There have been 201 patients with syphilis, 454 with gonorrhea, and 114 with both syphilis and gonorrhea. By Oct. 19, 1943, 409 patients had been discharged. At the Meridian center, 34 cases of early syphilis received the 5-day intravenous drip treatment, the other cases being given the 10-weeks' intensive therapy.

The majority of the patients admitted to the rapid treatment centers are young, immature girls of high school age, stranded wives of service men, or rural girls who have failed to cope properly with social life away from home. These individuals have responded favorably to the well-rounded rehabilitation program conducted by the State, which includes personal counseling, vocational training, and job placement.

**Venereal disease termed by Government biggest health menace to U. S. Armed Forces.** Editorial. Puerto Rico World Journal, Nov. 12, 1943.

A policy for the control of venereal disease in Puerto Rico, drawn up by the Interdepartmental Committee on Venereal Disease in collaboration with medical advisors of the Joint Anglo-American Caribbean Commission and the chief Army and Navy medical officers assigned to the Puerto Rico area, has been released through the local office of Community War Services of the Federal Security Agency.

The seven main points covered by these recommendations are: (1) The presence of venereal disease in any organization is called fundamentally a problem of command and, medically, a problem of preventive medicine. (2) Recreational facilities and a normal social life should be provided. (3) The United States Public Health Service, cooperating with the Pan-American Sanitary Bureau and Anglo-American Commission, should stimulate provision of facilities for control of venereal disease in the civilian population. (4) Health laws and regulations relative to venereal disease should be revised. (5) Survey of police methods should be made. Repression of prostitution in areas controlled by the United States should be pushed as "rigorous enforcement for the repression of prostitution has been demonstrated by experience to be the most effective method of reducing venereal infection." (6) Vocational training of girls should be undertaken. (7) Medical care for merchant seamen on shipboard should be provided.

High ranking Government officials have endorsed this policy. A full text of the statement of policy is given.

**Immediate wartime outlook and indicated post-war conditions with respect to the control of venereal diseases.** Thomas B. Turner. Am. J. Pub. Health, New York, 33: 1309-1313, Nov. 1943.

The author reviews the accomplishments in the control of venereal disease





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# Combined Artificial Fever and Aldarsone in the Treatment of Neurosyphilis<sup>1</sup>

A. E. Bennett, M. D., W. H. Morrison, M. D., H. C. Modlin, M. D.,  
Omaha, Nebraska

The continued search for better therapeutic agents in neurosyphilis led us, in 1940, to investigate the syphilitic properties of aldarson. Since 1934 we have used, in the fever therapy department of the University of Nebraska, the method of artificially induced fever combined with an arsenical for treatment of neurosyphilis. Our results with mapharsen have been reported previously (1, 2, 3). The purpose of this paper is to evaluate results of treatment with aldarson combined with fever and to compare them with those from mapharsen therapy.

## PHARMACOLOGY

Aldarsone is a pentavalent arsenical corresponding to the formula sodium-methylene-sulfon-amino-hydroxy-phenylarsonate. As described by Raiziss, Severac and Kremens (4) in 1934, it is freely soluble in water but insoluble in ether, acetone or chloroform. Its pH is 7.6 and it does not require neutralization with an alkali. The tolerated dose per kilogram in rats and rabbits is less than that of tryparsamide but higher than that of arsanic acid, acetarsone, or treparsol. The spirochetocidal power of the drug when injected intratesticularly is superior to that of tryparsamide (4).

## LITERATURE

The first clinical report on the use of aldarson in neurosyphilis was made by Kamman (5) in 1938. He gave 1,500 in-

jections of aldarson to a group of 53 patients, 40 of whom had had previous chemotherapy. Clinical diagnoses included asymptomatic, early parietic, taboparietic, tabetic, and meningovascular syphilis. From the clinical standpoint 27.5 percent unimproved by previous treatment improved with aldarson, and 30 percent improved by previous treatment obtained further improvement with aldarson. Toxic reactions occurred in 7 patients. In 3 cases constricted visual fields enlarged under aldarson therapy and in 2 cases constricted fields became slightly worse. In no case was aldarson discontinued because of eye changes. Statistics did not include the percentage of complete serologic reversals or the degree of clinical improvement.

A survey of 5 years' experience with aldarson in 133 neurosyphilitic patients was made by Spiegel, Liefer and Sarason (6) in 1941. Their cases included paresis, taboparesis, tabes dorsalis, vascular, meningovascular, and asymptomatic neurosyphilis. They found clinical improvement in 71 percent of 14 parietics, 53 percent of 28 tabetics, 33 percent of 6 taboparietics, 86 percent of 29 meningovascular parietics, and 46 percent of 28 optic atrophies. All 4 vascular cases improved. Of the 28 patients with optic atrophy not one showed improvement in blood or spinal fluid serologic reactions, but gratifying clinical changes were noted: Two obtained marked objective and subjective visual improvement; 11 had some enlargement of visual fields, and 12, of whom 3 had had field constriction with tryparsamide, had no progression of eye changes. Aldarsone was discontinued in one patient in whom amblyopia had developed

<sup>1</sup>From the University of Nebraska College of Medicine Fever Therapy Research Department. Read by title at the Central Society for Clinical Research, Chicago, Illinois, Nov. 5, 1943.

<sup>2</sup>We are indebted to Dermatology Research Laboratories and Dr. G. W. Raiziss for supplying aldarson for this study.

with tryparsamide and who complained of further dimness of vision after two injections of alvarsone. Serologic changes are given in detail below.

MATERIALS AND METHODS

Our report concerns 23 patients from the University of Nebraska College of Medicine fever therapy department and 21 patients from the Lincoln State Hospital, a total of 44. Diagnoses included general paresis, juvenile paresis, taboparesis, and meningovascular neurosyphilis. Because of incomplete or inadequate treatment and unsatisfactory follow-up studies in a shifting wartime population, we are reporting complete clinical and serologic studies in only 25 patients.

In this group fever was induced by the air-conditioned cabinet, or hypertherm. Treatment consisted of 50 hours of fever above 105° F. given in 3-hour sessions every 5 to 7 days, a total of 16 to 17 heatings. Bismuth salicylate, 0.01 gm., was administered intramuscularly just before each treatment and alvarsone was given intravenously at the height of the fever. With the first heating 0.25 gm. was used, 0.5 gm. with the second heating, and 1.0 gm. after that.

It was possible to study the progress of the University patients in some detail through routine neurologic, psychiatric, and ophthalmologic examinations, and blood and spinal fluid serologic tests. Visual fields were reexamined after the first, third, twelfth, and final treatments.

Spinal fluid serologic tests and electroencephalographic studies were made prior to treatment, after the twelfth treatment and again at the end.

In some instances the clinical and serologic improvement obtained after 12 treatments, or 36 hours of fever, was sufficient to discontinue fever therapy. Follow-up chemotherapy with alvarsone or other heavy metals and appropriate serologic check ups were routinely advised. Detailed study was not feasible with the State Hospital cases, but follow-up serologic and eye examinations were done in most instances.

It is not the purpose of this paper to discuss changes seen in electroencephalographic examinations in paresis; the value of this procedure was noted in a previous report (7). Its usefulness in diagnosing asymptomatic and prearetic cases and in following therapeutic progress of all parietic cases makes it a valuable adjunct to the research and clinical armamentarium.

CLINICAL RESULTS

Adequate follow-up studies and clinical evaluations were made for 25 patients, 18 from the University Hospital groups and 7 from the State Hospital group. The degree of improvement, as tabulated in table 1, was graded "A" for full clinical remission with return to former economic status; "B", partial improvement, and "C", little or no improvement.

TABLE 1

	Paresis			Juvenile paresis			Taboparesis			Meningo-vascular			Total
	A	B	C	A	B	C	A	B	C	A	B	C	
University Hospital.....	4	-----	3	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
State Hospital.....	4	8	2	-----	-----	2	-----	-----	1	1	-----	-----	-----
Total.....	8	8	5	-----	-----	2	-----	-----	1	1	-----	-----	-----

Clinical results:  
Paresis (21 cases):  
    "A" result—38 percent  
    "B" result—38 percent  
    "C" result—14 percent  
    Death (2)—10 percent

Most of the paretics from the University group were early cases while those from the Lincoln group were advanced cases requiring State hospital commitment. Both patients with juvenile paresis showed some improvement in social adaptability but remained mentally defective and were classified as "C" results. Of 5 cases diagnosed as taboparesis in the total of 44 analyzed, complete follow-up studies were possible for only one.

Of the 25 patients, 12 had had prolonged previous therapy, 7 had had none, and 6 had had a little. One patient, unimproved after 12 malarial chills, was a "C" result after fever and alvarsone, despite complete reversal of spinal fluid reactions. Another, unimproved after 10 inoculations of typhoid and 3 of pyripher, was classed as a "C" result after combined therapy, although all spinal fluid reactions showed improvement.

The figures in table 1 compare favorably with those for fever and mapharsen in our department (3). In that group of 9 cases of dementia paralytica 53 percent showed "A" results, 28 percent "B" results, and 18.5 percent "C" results. It is difficult to compare our figures with those of Kamman and of Spiegel and his coworkers because they do not rate the degree of clinical improvement. Kam-

man obtained some remission in 57.5 percent of all his patients and Spiegel 71 percent improvement in paretics. In both these papers the majority of paretics reported were early cases while over half of ours were advanced cases. Of 9 early cases in our present alvarsone group, 7 showed "A" results (78 percent), 1 "B" results (11 percent), and 1 "C" results (11 percent).

The superiority of fever therapy over all previous methods of chemotherapy is a generally recognized fact. An increasing number of reports in the literature emphasize that the best results in neurosyphilis come from combined fever and chemotherapy (8, 9). Studies made thus far of the effect of alvarsone used alone present no facts to change our conviction that the combined fever and heavy metal therapy is still superior to other forms of treatment in neurosyphilis.

From present indications, the type of arsenical used in the combined treatment does not materially affect the results. In addition to our previous reports on fever with mapharsen (3), Ewalt and Ebaugh (10) have made similar studies on the use of tryparsamide. The comparative figures of these three forms of treatment in dementia paralytica are given in table 2.

TABLE 2.—Comparative clinical results of fever with arsenicals

	Number of cases	Clinical results—Dementia paralytica				
		A	B	C	Died	Total improved
		Percent	Percent	Percent	Percent	Percent
Mapharsen and fever (2,3).....	70	53	29	18	-----	82
Tryparsamide and fever (8).....	134	19	50	22	9	69
Alvarsone and fever.....	21	38	38	14	10	76

If the normal percentage of error in comparative statistics and the personal equation in grading results are allowed, these figures show no definite superiority of one arsenical over another when used in combination with fever. Their effectiveness when given alone may be quite different.

#### SEROLOGIC RESULTS

Adequate follow-up studies of cerebrospinal fluid were made on 25 patients, 7 from the University group and 18 from the State Hospital group. For statistical presentation the 25 cases have been divided into those with follow-up studies



for more than 3 months after completion of fever and those with less than 3 months. Without exception every patient had positive blood and spinal fluid Wassermann reactions and paretic gold curve before treatment.

TABLE 3.—*Cerebrospinal fluid results in 12 cases with more than 3 months' follow-up study*

	Wassermann		Colloidal gold		Complete reversal	Partial reversal	Total	
	Negative	Less positive	Negative	Less positive			C. S. F. improved	C. S. F. not improved
Paresis: 10 cases.....	5	-----	5	2	3	5	8	
Juvenile paresis: 2 cases.....	1	-----	1	-----	1	-----	1	

TABLE 4.—*Cerebrospinal fluid results in 13 cases with less than 3 months' follow-up study*

	Wassermann		Colloidal gold		Complete reversal	Partial reversal	Total	
	Negative	Less positive	Negative	Less positive			C. S. F. improved	C. S. F. not improved
Paresis: 8 cases.....	4	-----	1	3	1	5	6	
Taboparesis: 4 cases.....	1	1	1	1	-----	3	3	
Meningovascular: 1 case.....	-----	-----	-----	-----	-----	-----	-----	

Serologic results—25 cases—tables 3 and 4:

Complete reversal (5)—20 percent  
 Partial reversal (13) —52 percent  
 Total improved (18) —72 percent  
 Unimproved (7) —28 percent

Similar detailed serologic studies were made by Spiegel and coworkers (6) in cases treated with aldarson alone; the comparative figures are given in table 5

TABLE 5.—*Serologic results from aldarson with and without fever*

	DEMENTIA PARALYTICA					TABOPARESIS					Number of cases improved
	Number of cases	Wassermann		Colloidal gold		Number of cases	Wassermann		Colloidal gold		
		Negative	Improved	Negative	Improved		Negative	Improved	Negative	Improved	
Aldarson alone: Spiegel, et al.-----	14	2	2	3	4	6	-----	1	-----	1	
Aldarson and fever: Present study.-----	18	9	1	6	5	4	1	1	1	1	

The striking difference between these two sets of figures shows clearly the value of combined therapy. The figures of 50 percent complete reversal of the Wassermann reaction and 50 percent improvement in colloidal gold tests are particularly noteworthy. These percentages will probably be improved when the 13 patients followed less than 3 months are rechecked at a later date.

We have also compared our aldarsones and fever patients with the mapharsen and tryparsamide groups previously re-

ferred to (8). The results are presented in table 6.

TABLE 6.—*Cerebrospinal fluid serologic results of fever and various arsenicals in dementia paralytica*

	Number of cases	Complete reversal	Partial reversal	Total improved
		Percent	Percent	Percent
Mapharsen and fever.....	70	34	37	71
Tryparsamide and fever.....	134	11	35	46
Aldarsones and fever.....	18	27	55	82

Little significant difference between the trivalent mapharsen and pentavalent aldarsones appears in this group of cases. However, subsequent serologic check ups on our aldarsones patients may improve these figures. Tryparsamide with fever lags behind the other arsenicals in producing serologic improvement. Tryparsamide used alone produces a higher percentage of clinical improvements than serologic reversals and apparently this action is still true when fever is added. In contrast, aldarsones and fever produce a much greater serologic improvement than aldarsones used alone or tryparsamide with fever.

Sixteen of the patients have had blood Wassermann check ups 6 months or more after completion of fever therapy. Five of these had reversal of the Wassermann reaction and one had a less positive reaction.

#### OPHTHALMOLOGIC COMPLICATIONS

In the total group of 44 patients, eye complications developed in 4 of the University group who had frequent checks of visual fields and ophthalmoscopic examinations.

One patient with taboparesis complained of blurred vision after 7 combined treatments, although objective examination was consistently negative. Aldarsones was discontinued after 11 heatings and 4 more heatings were given with a trivalent arsenical; the complaints stopped.

In one patient decreased visual acuity, field constriction, and bilateral optic

atrophy developed after 12 combined treatments. Examination a month after fever therapy was completed disclosed moderate bilateral optic atrophy, slightly constricted fields, and a drop in visual acuity from 20/20-20/20 to 20/30-20/50.

In another patient dimness of vision developed after 8 treatments; ophthalmoscopic examination disclosed pallor of the left optic disk. The patient died a few days later of other complications.

One patient experienced sudden loss of vision in his left eye after 10 combined treatments; a diagnosis of retrobulbar neuritis was made. Later, visual acuity in this eye improved to finger counting and the optic disk became gray.

The 21 patients from the State Hospital group did not have routine field and ophthalmoscopic examinations, and the evaluation of the effects of aldarsones and artificial fever on their optic nerves must be empiric. No subjective complaints came from any patient and check-up ophthalmoscopic examinations of many patients at completion of fever therapy revealed no abnormalities of the fundus. Paroled patients have all returned to their former social and economic status and presumably have noted no visual handicaps. Those not paroled, under constant medical observation, have given no evidence of visual impairment.

The previous reports of 186 patients treated with aldarsones alone by Kamman and by Spiegel, Liefer and Sarason included only one patient whose eye changes necessitated discontinuing aldarsones; he had had preliminary eye damage from

tryparsamide. Since the chief disadvantage of tryparsamide has been ophthalmologic complications, demonstration of a clinically and serologically effective pentavalent arsenical without such dangers will be a valuable contribution to syphilitic therapy. One of our patients who had had field changes and decreased visual acuity after 26 tryparsamide injections experienced no eye changes with a full 50 hours of fever and 17 aldarsonic injections. Another patient who had had field changes after 3 tryparsamide injections has had no untoward effects after 7 aldarsonic injections without fever.

It is probable that in some neurosyphilitic patients the optic nerves will always be susceptible and sensitive to arsenicals in clinically effective doses, and therefore complete safety in this regard may be difficult to attain. Only certain radicals (9) of the organic arsenical have been supposed to effect the optic nerve specifically, but every known pentavalent arsenical tried thus far has caused changes of the optic nerve under some conditions. Aldarsonic possibly may be a relatively safe drug when used alone, but in our hands, when combined with fever, it has caused serious ophthalmologic complications and must be used with considerable caution.

#### OTHER COMPLICATIONS

There were 2 deaths in our group of 44 cases, both from complications of treatment. One patient, included in the ophthalmologic complications, in addition to optic atrophy, suffered a series of intestinal hemorrhages after his ninth treatment; autopsy showed an acute duodenal ulcer. The other patient, in whom a severe toxic arsenical reaction developed with hepatitis, nephritis and exfoliative dermatitis, died 6 months later in a State hospital.

The only involvement of the nervous system, except for changes of the optic nerve, occurred in the patient with retrobulbar neuritis reported above. Concomitant with the eye changes, sacral anesthesia developed, and later weakness, anesthesia and decreased reflexes in both

legs, with sphincter paralysis. Another patient, 71 years of age and arteriosclerotic, had a grand mal attack during the sixth treatment; presumably a pyrexial rather than an arsenotoxic reaction. The patient's generally debilitated condition caused us to discontinue all treatment except iodides.

One patient in whom an arsenical dermatitis developed after 8 treatments received an additional 8 fever and aldarsonic treatments without difficulty after 5 weeks' rest. In still another patient, with skin sensitivity to neoarsphenamine, a dermatitis developed after 3 injections of aldarsonic without fever.

#### SUMMARY

The pentavalent arsenical, aldarsonic, combined with artificially induced fever has been investigated from the clinical standpoint for the treatment of neurosyphilis. Forty-four patients were given artificial fever by an air-conditioned cabinet, combined with intramuscular injections of bismuth just prior to heating and intravenous injections of aldarsonic at the height of the fever. Complete results are presented for 25 patients.

Twenty-one cases of paresis were treated, and of these 38 percent obtained "A" results (full remission), 38 percent "B" results (partial improvement), and 14 percent "C" results (no improvement). Ten percent of the patients died. Two cases of juvenile paresis and one of taboparesis gave "C" results and 1 case of meningovascular neurosyphilis gave an "A" result.

Serologic improvement was gratifying. After treatment, 50 percent of the patients had a negative spinal fluid Wassermann reaction and 60 percent had improvement in the colloidal gold curve. Complete spinal fluid reversal occurred in 20 percent and partial reversal in 52 percent, a total of 72 percent. Of 17 paretics, 82 percent improved. These results are much better than those with aldarsonic alone or fever with tryparsamide; they are slightly better than with fever and mapharsen. Of 16 patients, 5 had com-



plete blood Wassermann reaction reversal and one was clinically improved."

Ophthalmologic complications occurred in 4 patients. One had subjective blurring of vision, 2 had primary optic atrophy, and 1 had retrobulbar neuritis with secondary atrophy.

Other complications were a bleeding peptic ulcer causing death of 1 patient after 9 heatings; nephritis and exfoliative dermatitis, ending in death of 1 patient, 6 months after treatment; grand mal seizure in 1 patient during the sixth heating; mild dermatitis in 2 patients, and damage to the spinal cord in the patient with retrobulbar neuritis.

CONCLUSIONS

- 1. Aldarsone is clinically effective in the treatment of neurosyphilis.
- 2. Combined artificial fever with aldarsone, or some other arsenical, is the treatment of choice in neurosyphilis because of the high percentage of clinical and serologic improvement.
- 3. Aldarsone, combined with artificial fever, produces neuro-ophthalmologic complications and should be used with considerable caution.

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# Gonorrhea: The Epidemic We Face

P. S. Pelouze, M. D.<sup>1</sup>

According to one of Webster's definitions, romance is a "dreamy, imaginative state of mind," though it is certain that he was not thinking of the treatment of gonorrhea when the definition was written. Romancing, according to him, is "To write or tell romances; indulge in extravagant stories." And here again he did not have in mind the numerous papers and statements that have appeared in scientific and lay publications on this subject.

There is nothing wrong with romance or romancing if he who reads or hears takes it for what it is. The trouble arises from getting the idea that he is being treated to *science* which, in its final analysis, should be *truth*. Truths are facts and in medicine facts should be based upon established things. They should not be founded upon dreams or even superficial observations if irreparable harm is to be avoided. Nowhere in all the field of medicine have fact and fancy been more thoroughly and more continually jumbled than is the case with gonorrhea and its treatment. Statements regarding the value of this or that treatment, often by those none too familiar with the disease itself, have appeared in our medical journals and later (sometimes before) in the lay press, until they have led the public to believe that gonorrhea no longer is a national problem, and the medical profession becomes temporarily enthusiastic, seemingly for purposes of later disappointment, often disgust.

It is not to be supposed that any great number of those who wrote medical articles about the use of the sulfonamide drugs in the treatment of gonorrhea were consciously romancing, but often the

product was just as misleading as though they were. Many of the articles showed an unfortunate lack of real knowledge of the cardinal principles of gonococcal infections. As the result of this, they fell into the rather common error of listing as "drug cures" a goodly percentage of patients who, though their disease might have been slightly influenced by the drugs, really owed their cure to the stimulation of native curative responses by local treatment, or to the fact that they eventually raised these responses spontaneously, as gonorrheics have done since the first gonococcus found the first urogenital mucous membrane. It is, and for some time has been, outstanding that the patient who carries the gonococcus beyond the first two weeks of sulfonamide medication is in no sense a "drug cure." He is either a local-treatment-stimulated cure or a self-cure. To call them all "drug cures" is to court romance.

Further, we have bandied around that word *cure* until many of us believe that all those patients whose symptoms have disappeared as the result of sulfonamide medication and who have passed beyond our observation were really cured. We have talked of pyretotherapy as though it, too, promptly *cured* all of the patients it rendered asymptomatic. We have talked of the glories of penicillin in the failures of the foregoing as though we had never a sorrow left; we have hardly paused to wonder for whom pyretotherapy was available or was not (mostly not), or who could get penicillin for the treatment of gonorrhea, or who could afford to pay for it if it suddenly were made commercially available. Most assuredly, he who thinks the time has not arrived for puncturing a host of therapeutic bubbles certainly has not traveled far

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from his own doorstep nor analyzed conditions as they now exist.

We are at war, and war always has greatly increased, and probably always will increase what some like to call illicit sexual contacts; such contacts spread gonorrhea, which always was one of the greatest causes of "lost man-days." We might get some idea of its comparative importance among the Armed Forces with that of syphilis by calling attention to the fact that, where such infections are reported to local health authorities by the Armed Forces for searching out sources, from 7 to 10 cases of gonorrhea are reported to every new case of syphilis—in one State, at least, the ratio varies from 15 to 30 of gonorrhea to a new one of syphilis. If we spread this to war industry, the importance of knowing just where we stand therapeutically becomes increasingly obvious. This is by no means reduced when we think in terms of society at large and those thousands of teen-age and older women who through superpatriotism (or something) "think that the least that they can do for those who are going to risk, perhaps lose their lives, is to minister to their 'creature comforts.'"

Time was, and not so long ago, when he who raised a voice against the run-away type of "scientific" investigation that put sulfonamides on the map so far as the treatment of this disease is concerned, was called some pretty harsh names. I know, because I admonished caution when I discussed the first paper read in this country on the treatment of gonorrhea with sulfanilamide. All I said was, "From a very limited experience with sulfanilamide I am afraid that if we are not very careful we shall look in vain for the hoped-for reduction in incidence." So guarded a statement as that made me rather unpopular in some quarters for a year or more until the awakening came. Now the American Neisserian Medical Society and a host of interested clinicians insist that this particular drug should not be used for the treatment of gonorrhea.

Then came the later sulfonamides and a number of investigative reports to the effect that they would cure 80 percent or more in 5 days. The idea gained general credence—I thought it was so myself until I saw where we had stubbed our collective toes. Many physicians believe it today, but it never was, and never will be, true. Of course, we are blaming our present-day awakening upon the hard-to-prove ideas that thousands of our citizens are being made "sulfaresistant" through the promiscuous use of drugs or that we are developing a lot of strains of gonococci that can "take" our sulfonamides and ask for more. These things may be true; it is also true that our numerical cure standards were decidedly inflated. Apparently we cannot do much about this sulfaresistance matter, but we could cut down our 80 percent yardstick to something nearer the real truth—say to about 60 to 65 percent under ordinary treatment conditions. And, also, as will appear later, we had better not be too sure that more than two-thirds of those patients are really *cured* when they seem to be. We may get better asymptomatic rates (commonly called "cure rates") by placing our patients in bed for the first 3 or 4 days of medication, and we will get far lower asymptomatic rates in individuals subjected to grilling periods of strenuous activity—such as soldiers on maneuvers and the like.

During the last 2 years I have talked with hundreds of physicians treating large numbers of patients for gonorrhea, and I have found no glowing optimism regarding those high percentages of cure. Almost to a man they have had a rude awakening. They are talking about 60 percent asymptomatic rates in males and less than 50 percent in institutionalized females. They are also making far less use of the word *cure*.

There are other factors at play in both asymptomatic rates and true cure rates. It is the general opinion in military circles that sulfathiazole is almost a specific for the Negro race; naturally, the



higher the percentages of Negroes in any treatment group, the higher the asymptomatic and, probably, the cure rate. In this regard early in the use of sulfathiazole, when gonorrheics were hospitalized, I was struck by the few Negroes with gonorrhea in military wards as compared with white patients, despite the higher infection incidence in the former. Inquiry among the medical personnel brought out the fact that on only a few occasions had it been found necessary to transfer Negroes from station to general hospitals for pyretotherapy; most of those so transferred were white men. Thus doctors in the South talk of higher cure rates than are found in the North, where the ratios between white and Negro troops usually are reversed. One group thinks itself better than the other, and the other wonders how it gets that way. Study of the comparative rates in the races would do much to encourage the low-cure-rate boys in the North.

I must admit that I have always been rather skeptical and somewhat concerned about sulfathiazole as a prophylactic—there was just a little too much of the unknown. My attitude was that when it could be shown that asymptomatic gonococcus carriers were not being made, I might grow a little more enthusiastic about sulfathiazole. I realized what a ticklish matter it was, and even now I feel it is unwise for me to go into details about the matter lest I shatter some highly valued friendships. I do think, however, the matter should be reinvestigated most carefully—it is far too important to be allowed to limp along as it is now. I am reliably informed that among the military personnel coming into one of our ports from a certain country approximately 90 percent of those who have gonorrhea had had sulfathiazole before and after exposure. The arresting part of this information was that none of the patients developed symptoms in less than 2 weeks after exposure and many of them not until 3 or 4 weeks had elapsed. If this is so, and I think it is, an investigator could be grossly deceived unless he had

his "guinea pigs" under close observation for at least a month, perhaps longer. To go completely overboard without such a restudy would hardly be in the interests of disease prevention.

So far as the question of gonorrhea prevention is concerned, there unquestionably is something in the general clinical picture which is heading us toward a real epidemic and which, in my opinion, will probably double within the next year some of the low incidence rates of which we now boast. The trouble rests in the frequent differences between asymptomatic rates and true cure rates. Gradually we are learning that those who said there was little or no asymptomatic gonococcus carrier rate among patients seemingly cured by sulfathiazole were somewhat in error, and the error in some groups may be as high as 32 percent.

It has been my good fortune to have had an opportunity to come into personal contact with those who did the clinical and laboratory work upon which the report of Koch, Mathis and Geiger (*Venereal Disease Information*, Feb. 1944) was based; I have seen neither better clinical work nor an investigative group with a better conception of the confusing factors which so commonly cause work on gonorrheal patients to be misleading. Among a mixed group (male and female) they were able to obtain positive gonococcus cultures in 32 percent of those rendered asymptomatic by one course of sulfathiazole.

One of our large naval hospitals, dealing solely with males, obtained a 23 percent positive culture rate among those rendered asymptomatic by sulfathiazole medication.

Reverting to the report of Koch, Mathis and Geiger, it is of interest to note that, within the first month after the positive culture, 47 percent had reached and held a culture-negative state; by the end of the second month, 34 percent more were negative; by the end of the third month, 14 percent more, and later, 5 percent still gave positive cultures.

There is no need to resort to a crystal ball in order to estimate what this means in terms of disease spread; there is not

the slightest reason to doubt that the gonococci of these asymptomatic individuals produce the disease when transmitted to other individuals. In many patients the duration of the carrier state is such as to offer us a terrific challenge in these days of ready assumptions of cure because all symptoms have disappeared. They call for patient control and patient instruction regarding the protection of others for far longer periods of time than generally are being carried out or revised. In no other way can we prevent the harvest of infection that is now in the making.

So far as civilian practice is concerned, the fumings of the lay press, and often of the medical press from which it frequently gets its ideas, have caused a complete reversal of the old order. Today the tablet is king and the physician is merely the means of obtaining the tablet. Particularly in the Southern and the Eastern States, the physician is not even thought of, and the druggist takes his place in a dangerous number of cases. Even in the Armed Forces it is often possible to circumvent the medical officers and to obtain enough sulfathiazole to at least hide symptoms. In other words, thousands upon thousands of patients make their own pronouncements of "cure" and blithely return to their former activities. This, of course, always occurred to some extent, but never in such proportions as now.

Someone once remarked that in every great advance there is always some loss. In former days, the physician and his local treatments amounted to something in the therapeutic picture. At least he was able to keep a large percentage of his patients under observation for a reasonable length of time and thereby did much to prevent disease spread. The case-holding value of gentle local treatment, so far as gonorrhea is concerned, is beyond dispute, and I am convinced that much was lost in epidemiologic values when it was so generally abandoned. Since I am not practicing for the duration, I do not think I can be accused of a monetary slant when I suggest that

we would increase our value to society at large and the war effort in particular if, in a large measure, we went back to where we were before we had sulfonamides, unless pyretotherapy is available and penicillin can be had, particularly at a cost low enough for the income of the group wherein most of the gonorrhea is found. In other words, we should get the mind of the patient upon the physician and his treatments and foster the view that the tablets are a valuable adjunct rather than the be-all and end-all of therapeutic endeavor.

In view of the rather high failure rate and the hidden but arrestingly large asymptomatic gonococcus carrier rate as the result of sulfonamide medication, local treatment in the male is indicated in at least 50 percent of the patients. Judged from the positive culture findings of the two investigative projects previously mentioned, the cases wherein such treatments have a true therapeutic value is probably around 75 percent. As cultures are not universally available, and without them one cannot say with even reasonable safety who is or who is not a "carrier," the field of epidemiologic values could be greatly enhanced if we raised the figure to 100 percent for most in civilian practice.

When one talks of local treatment for gonorrhea in the male it goes almost without saying that he means sensibly planned and carried out measures, utterly devoid of trauma and the high pressure of fluids that do so much toward spreading the infection into structures where it otherwise seldom would enter. It was the unskilled and injudicious application of local treatments that did so much to discredit them. Few who used local treatments properly could deny that they promote curative effort on the part of the patient and, in the final analysis, the patient was the one who produced the cure—we helped or hindered him depending upon what we did and how we did it. The definite sulfonamide failure needs local treatment. The carrier state will be greatly shortened by it, society needs it for its case-holding value at least, and I



can conceive of no other way by which the physician can take his rightful and highly needed place in the unfortunate scheme of things as they now exist. To let scientific but unavailable possibilities serve as our justification for following the course of least resistance (and bother) is to miss the mark. The millennium for the gonorrheic is not yet with us to the extent that we should further foster in him the present miracle-tablet-worship while we go no farther than "the laying on of hands"—if we do even that.

Before we return to local treatments, however, there is a crying need for an understanding of the underlying principles of gonococcal infections. Without it, the physician blunders in his local treatments, but with it he is a gift to his patient and need make no apology to society.

Above all let us realize that, as things are at present, we already have started toward the greatest epidemic of gonorrhea that our country has ever experienced. Whether we reap its full harvest or check it depends solely upon what we do about the matter and how we do it. It is not alone the problem of the Armed Forces and the Public Health Service; it is the problem of society at large and the medical profession in particular. We can check this epidemic if we will.

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## DIAGNOSIS

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**The clinical diagnosis of uncomplicated syphilitic aortitis.** Paul E. Mattman and Joseph Earle Moore. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, 27: 711-715, Nov. 1943.

Uncomplicated syphilitic aortitis is often an asymptomatic disease, but the extent to which this is true varies with two factors: (1) The extent of pathologic damage to the aorta, and (2) the care devoted to history taking and physical

and laboratory examination of the patient.

In diagnosing uncomplicated syphilitic aortitis in a patient with known late syphilis in whom hypertension, extensive arteriosclerosis or rheumatic heart disease are not present, the following symptoms and signs should be looked for: Roentgenologic demonstration of dilatation of the first portion of the aorta, heart failure or lowered cardiac reserve in the absence of hypertension or valvular disease, localized substernal pain (to be differentiated from anginal pain), and characteristic changes in the second aortic sound.

In 1932, Moore, Danglade and Reisinger pointed out that at Johns Hopkins Hospital in 105 patients found at necropsy to have syphilitic aortitis uncomplicated by aortic regurgitation or aneurysm, the clinical diagnosis had been correctly made or suspected before death in only 17 instances (16 percent). The authors are now reporting on an additional 79 patients dying in the Johns Hopkins Hospital from 1932 to 1941. Comparing the medical cases in the two groups, it is seen that in 41 percent of those in the first series and 68.1 percent of the second series, the diagnosis was correctly made or suggested during life. This suggests that not only are the criteria of diagnosis valid but also that there is a keener appreciation of them than was formerly the case.

**Acute syphilitic meningitis: A clinical study of fifteen cases.** John E. Skogland. *South. M. J.*, Birmingham, 36: 809-815, Dec. 1943.

Acute syphilitic meningitis is a comparatively rare complication of syphilis. It is usually associated with acquired syphilis and may appear at any stage of the disease, but more often within a comparatively short time after the initial infection. Patients who develop acute syphilitic meningitis usually have had no previous treatment for syphilis or have been inadequately treated. The blood



Wassermann reaction is negative in approximately one-third of the cases.

The pathologic change encountered in acute syphilitic meningitis is thickening of the meninges. Cases of acute syphilitic meningitis can be classified in the three groups of acute syphilitic hydrocephalus, acute syphilitic meningitis of the vertex, and acute syphilitic meningitis, basilar type. Fifteen cases illustrating these three different types of the condition are analyzed by the author. One case is reported in detail.

The treatment varied widely in the cases reported. No deaths occurred. The acute symptoms responded readily to antisyphilitic drugs. Trivalent arsenic initially was the treatment of choice, using alternating courses of one of the heavy metals and arsenic until outward signs of the syphilitic infection disappeared and serologic reactions became negative. Pentavalent arsenic may be substituted for the trivalent compound if the clinical response is unsatisfactory or if abnormalities in the cerebrospinal fluid fail to subside appreciably. Fever therapy may be given if cerebrospinal fluid abnormalities persist. The patients usually recover, but sequelae, such as cranial nerve palsies or diverse focal defects, may occur.

The case described by the author was one of syphilitic meningomyelitis occurring as an end-result of acute syphilitic meningitis. The patient was first seen in 1932, when a diagnosis of acute syphilitic meningitis was made. His symptoms promptly disappeared following the oral administration of potassium iodide and a single injection of bismuth. He failed to return for further treatment until 1939, when for 2 years he received weekly treatments. Weakness of the lower extremities progressed and impotency and frequency of urination increased. He returned to the hospital in 1942. The only cranial nerve abnormality was pupillary irregularity and incomplete reaction to light. He was not able to walk without support because of a moderately severe spastic paraplegia. Blood and spinal fluid tests were negative for syphilis. No

further change was noticed in his condition when he was seen in April 1943.

**Report of reexamination of 4,994 men disqualified for general military service because of the diagnosis of cardiovascular defects.** Robert L. Levy, William D. Stroud and Paul D. White. J. A. M. A., Chicago, 123: 937-944, 1029-1035, Dec. 11 and Dec. 18, 1943.

Following a statistical survey made by the Selective Service System, it was found that the group disqualified for disorders of the heart and circulation accounted for approximately 10 percent of all rejectees. Since this rate seemed excessive for men between the ages of 18 and 38 years, the Subcommittee on Cardiovascular Diseases of the National Research Council recommended a project for the reexamination by boards of cardiologists in each of 5 cities in which 1,000 registrants had been rejected for cardiovascular reasons. Boston, Chicago, New York, Philadelphia, and San Francisco were chosen because of their facilities for examination and study. Examinations were carried out in large general hospitals and the criteria of admissions to the Army were followed as outlined in Mobilization Regulations (MR) 1-9, paragraphs 60-67.

The total number of rejectees examined was 5,127, of which 4,994 were included in the final statistical study. The majority of the men were white but of a great variety of national stocks. The number of Negroes varied with the different cities, and there was a high percentage of rejections among them, as well as among the Chinese and the few Filipinos.

Nine tables of analysis of these reexaminations are given. From the table showing the result of examination according to original rejection diagnosis, by local board or induction station, it is seen that there were 5 rejections for syphilis of the aorta out of a total of 4,035 cases examined and 3,446 rejections in the 4 cities of Boston, Chicago, New York, and Philadelphia, 2 being from Boston and 3 from Philadelphia. There was 1 case of aneurysm of the aorta (from New York). In the

table showing final diagnoses of cases rejected by special boards, there are 17 cases of syphilis of aorta, 5 from Chicago (0.5 percent of its cases finally rejected), 7 from New York (0.9 percent), 3 from Philadelphia (0.3 percent), and 2 from San Francisco (0.3 percent). There were 6 white and 9 Negro rejections from the first 4 cities.

The more important results of the re-examination are discussed in the second paper.

In the 17 cases of syphilis of the aorta, aortic regurgitation was found in 5 cases, aortitis without aortic regurgitation in 7, and in 5 the lesion was not specified. No syphilitic cases were found in Boston, where only 23 Negroes were examined in contrast to the 90 Negroes in New York and 207 in Philadelphia.

**Yaws: Report of a case appearing in a white man.** Jack Kinell. U. S. Nav. M. Bull., Washington, 42: 187-192, Jan. 1944.

While the incidence of yaws is very high among the natives of the islands of the South Pacific, no case of yaws or anything resembling it had been observed among the troops in this area 17 months after their arrival there. The author reports a case, however, which shows that white men are not immune to this tropical disease.

The patient was a 20-year-old staff sergeant, American born of Italian parents. He denied the possibility of a syphilitic infection, and a month prior to admission a blood Kahn reaction was negative. He had never been on duty which brought him in close contact with the natives, but he had occasionally fondled native children and visited with native friends. He denied sexual intercourse with native girls. Because of his work he practically always had minor cuts and scratches on his hands, and he complained that flies in the area were a continual annoyance.

About 4 months before coming to the hospital the patient had noticed a pain-

less "sore" on the flexor surface of the right wrist, which treatment failed to heal. A month later a painless, incrustated nodule appeared on the penis, and later similar lesions were seen in the gluteal furrow, on the right hand, the left popliteal space, soles of both feet, the cheeks and chin. His blood tests were strongly positive for syphilis and repeated dark-field examinations of the serum from the lesions were positive for spirochetes morphologically identical with *Treponema pallidum*. Biopsy of specimens showed histologic changes identical with those seen in several proved cases of yaws and consistent with the diagnosis of this disease.

At the time of transfer of the patient to another activity after 21 days of treatment with neoarsphenamine intravenously and bismuth salicylate intramuscularly, all lesions were healed.

**Electroencephalographic diagnosis of organic brain disease.** Clifford G. Hines, Luman H. Tenney and Joseph Hughes. U. S. Nav. M. Bull., Washington, 42: 101-107, Jan. 1944.

From a clinical viewpoint, the electroencephalogram (EEG) is a record of the electrical activity of the ganglion cells in the gray matter of the cortex. It is of the greatest value in the diagnosis of cortical lesions and as such it becomes an intricate part of the psychiatric and neurologic examinations. Its diagnostic aid was evidenced in this study by an acceleration of the diagnosis and the onset of therapy and a shortened period of hospitalization.

The EEG findings were studied in a group of 205 patients with various neurologic conditions. In this group were 6 patients with neurosyphilis and in 5 of these the EEG findings were positive. The EEG for a patient whose chief complaint was nervousness, headaches, left-sided Jacksonian seizures is reproduced. It showed abnormally low voltage waves in both hemispheres, and a diagnosis of central nervous system syphilis was made.



**Trichomoniasis in the male. A seventh venereal disease?** Gordon G. Allison. South. M. J., Birmingham, 36: 821-823, Dec. 1943.

Until recently the medical profession has considered trichomonad infection of the male to be a rare condition. The ability to recognize trichomonads in a stained specimen has changed this attitude. The Georgia State Board of Health Laboratories have devised the Sellers Negri stain, which is a superior method for the identification of the trichomonas. This method and the preparation of the stain are given in detail.

In the female it is common practice to search for the living trichomonads when vaginal itching, burning, and frequency of urination is present. This organism should also be looked for in the male urethra where urethral itching and a milky, watery discharge is found, particularly in the absence of gonococci and *Treponema pallidum*.

Trichomoniasis in the male has been reported by various investigators. In his private practice, the author has found an incidence of 15 percent, all white patients. The organism was independent of the gonococci, and found in the prostatic and seminal vesicular secretions. The method of isolating the organism in the male is described.

Sellers and Reynolds of the Georgia State Board of Health Laboratories report that in a total of 2,980 urethral and vaginal spreads examined for gonorrhea, 528 from female patients were found to disclose *Trichomonas vaginalis*, and 17 from male patients. Patients were both white and Negro.

Usually trichomoniasis does not occur in a patient unless he has stricture of the urethra or poor drainage of the canal. Topical application of silver nitrate to the veru, permanganate irrigations, acriflavine instillations, and acidulation of the urine are usually effective.

During the past 4 months the Medical Department of the Army has rejected a large number of Negro draftees for trichomoniasis, which leads the author to conclude that this condition is considered a venereal disease by the Army.

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## TREATMENT

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**New chemotherapeutic agents in the treatment of infectious diseases—sulfamerazine and sulfamethazine.** Harry F. Dowling. M. Ann. District of Columbia, Washington, 12: 467-471, Dec. 1943.

The author summarizes his experiences with sulfamerazine and sulfamethazine. A total of 183 patients with various types of pneumonia and meningitis, staphylococcal bacteremia, subacute bacterial endocarditis and other infectious diseases was treated with sulfamerazine; 24 of these patients died. An additional group of 57 patients with gonococcal arthritis, pyelitis, lung abscess, and bacillary dysentery was treated with this drug. The results in these patients were comparable to those found from the use of sulfapyridine, sulfathiazole or sulfadiazine. It is therefore concluded that sulfamerazine possesses efficacy equal to that of most of the currently used sulfonamides in the treatment of many infectious diseases, that it apparently does not cause fewer toxic reactions than sulfadiazine, and that it has the advantage of slower excretion. Although sulfamerazine is not likely to displace sulfadiazine and sulfathiazole it will probably take its place with them.

A total of 59 patients suffering from pneumonia, bronchitis, gonococcal arthritis, pyelitis, bacterial endocarditis and lung abscess was treated with sulfamethazine. Five of these patients died. Because of the small number of patients it can only be surmised at the present time that the toxicity of sulfamethazine is in general comparable to that of sulfadiazine and sulfamerazine. Of the patients treated, 11.9 percent had severe toxic reactions from sulfamethazine.

It was found that the absorption of sulfamethazine was very irregular. Initial doses of 4 gm. followed by 1.5 gm. every 4 hours produced average blood levels of free sulfamethazine anywhere



from 2.9 to 13.9 mg. per 100 cc. In the same patient these levels varied as much as 16 mg. per 100 cc. from day to day.

**Penicillin therapy in sulfonamide-resistant gonorrhea in men.** C. J. Van Slyke, R. C. Arnold and M. Buchholtz. *Am. J. Pub. Health, New York, 33: 1392-1394, Dec. 1943.*

The authors, in collaboration with Mahoney, have previously reported their findings in 75 male patients with sulfonamide-resistant gonorrheal urethritis treated with penicillin, 74 of whom were cured. They now report further studies on 5 additional patient groups (103 patients). In these 5 groups the minimum amounts of the drug and the shortest treatment period which would produce an acceptable cure rate were considered, using varying schedules of dosage and treatment periods.

The first group comprised 23 patients, 21 of whom had not responded to previous sulfonamide therapy. Each received 5 intramuscular injections of 20,000 units of penicillin at 3-hour intervals, a total dosage of 100,000 units being given over a 12-hour period. All of the patients in this group satisfied the criteria of cure and in follow-up observations, in some instances as long as 14 weeks, did not show any tendency toward a recurrence of symptoms.

The second group comprised 25 patients, 8 of whom had not received sulfonamides. The total dosage was 100,000 units, given in injections of 25,000 units at 3-hour intervals, over a 9-hour period. In this group, 21 were cured and 4 were failures.

The third group comprised 25 patients, 6 of whom had received no sulfonamide therapy. Injections of 15,000 units were given at 3-hour intervals, until a total dosage of 75,000 units was reached, covering a 12-hour treatment period. One failure was reported.

The fourth, a group of 15 patients, 13 of whom were sulfonamide-resistant, received injections of 10,000 units at 3-hour intervals, until a total dosage of 50,000 units was reached, covering a 12-hour treatment period. Three failures were

reported, 2 of whom were given a total of 120,000 units a few days later and pronounced as cured.

The fifth group of 15 patients, 11 of whom were sulfonamide-resistant, received a total dosage of 120,000 units in 6 injections over a 15-hour treatment period. All of these patients were cured.

From their results, the authors conclude that one optimal treatment routine calls for 120,000 units of penicillin, over a 15-hour period. A second routine could call for 50,000 units, as given in the fourth group. However, further study is necessary before final conclusions can be reached. No difference has been found in the response of gonococcic infections to penicillin between untreated patients and those who had failed to respond to the administration of sulfonamides.

#### **Therapy with sulfonamide compounds for patients with damage to the liver.**

Osler L. Peterson, Emmanuel Deutsch and Maxwell Finland. *Arch. Int. Med., Chicago, 72: 594-612, Nov. 1943.*

During 1941 and the first 6 months of 1942, at the Boston City Hospital, the authors studied the effects of sulfonamide treatment on the clinical course and hepatic function in 37 patients with various types of liver damage.

Patients with acute hepatitis associated with bacterial infections showed excellent results from sulfonamide therapy, improvement in hepatic function paralleling that in the underlying infection. In patients with chronic damage to the liver, hepatic dysfunction was not increased by sulfathiazole or sulfadiazine. Some improvement was seen in cases in which bacterial infection was aggravating the hepatic injury.

The authors warn against the use of the sulfonamides in patients with portal (Laennec's) cirrhosis. Extreme caution should be taken when administering the drug as the toxic effects other than direct injury to the liver occurring in these patients were unusually frequent, and were twice as common after sulfathiazole as after sulfadiazine.

From their observations, the authors conclude that the presence of damage to the liver should not be considered as a contraindication to sulfathiazole or sulfadiazine therapy in patients with bacterial infections against which these drugs are effective..

**Renal complications of combined sulfathiazole-fever therapy.** Arthur M. Pruce and Benjamin H. Lennon. Arch. Phys. Therapy, Chicago, 24: 721-724, Dec. 1943.

In a series of 250 soldiers with artificial fever and concurrent sulfathiazole therapy at Stark General Hospital, only 3 had transitory renal damage. Case reports are given on these 3 patients.

Prior to the fever session, a routine dose of 12.5 gm. of sulfathiazole with sodium bicarbonate gram for gram was administered to 200 patients, the doses being divided over the 48-hour period. The last 50 patients were given a total dose of 9 gm. over an 18-hour period, in compliance with instructions from the Office of the Surgeon General of the U. S. Army.

Laboratory studies included phenolsulfonphthalein excretion tests; determination of the blood levels of nonprotein nitrogen, total chlorides and sugars; urethral spreads, and prostatic cultures. If the routine urine examination, which is considered the most important single laboratory procedure, shows erythrocytes, albumin, and sulfa crystals during the administration of sulfathiazole, combined fever therapy is contraindicated.

Eight hours of fever at a temperature level of 106° to 106.7° F. induced in 90 minutes proved to be an effective dose. To secure an adequate fluid balance during therapy, 6 liters of fluid per day were given for 2 days before treatment, an average of between 4 and 5 liters during the session, and 2 liters in the first 6 hours after therapy. The fluid intake and urinary output were carefully charted. To the most recently treated patients, 10 gr. capsules of sodium chloride (8-12 gm.) have been administered during the fever session; this resulted in decreased

gastric irritation, nausea and vomiting.

At Stark Hospital, one-third of all patients with gonorrhea who were given sulfathiazole alone showed sulfa crystaluria, with evidence of mild renal damage in about 1 percent of these cases. The incidence of renal complications with the combined therapy was similar to that with sulfathiazole alone.

The authors believe that the combination of sulfathiazole and artificial fever therapy is relatively innocuous provided proper precautions are taken.

**Recent advances in clinical ophthalmology.** John E. L. Keyes. Ohio State M. J., Columbus, 39: 1110-1112, Dec. 1943.

Comparing the two most recent therapeutic agents used in the treatment of ocular diseases, penicillin and sulfonamide compounds, the author states that the ultimate usefulness of penicillin has not yet been established. However, enough therapeutic evidence has been accumulated to indicate that in certain ocular diseases penicillin is undoubtedly a drug of choice, and research being carried on at Bushnell General Hospital strongly suggests that it will be efficacious in other eye diseases.

Penicillin has been found to be particularly useful locally and systemically in gonococcal infections. Therefore, parenteral treatment of eye diseases with penicillin should supplement local instillations in gonorrheal ophthalmia in infants or adults.

Because of the bacteriostatic action of penicillin in weak concentrations, it is necessary to keep the patient well saturated systemically and/or to use topical applications frequently. Insufficient dosage may result in the treated organism becoming penicillin-fast and to date no method of resensitization has been evolved. Solutions for instillation in the eyes should not exceed 250 to 1,000 Oxford units per 1 cc. due to scarcity of the drug; solutions up to 5,000 units per 1 cc. have been used without harmful results. The present practice is to instill 2 or 3 drops of penicillin solution as frequently as every hour



or, in severe cases, every half hour. Intravenous and intramuscular dosages of penicillin range from 5,000 units to 15,000 units, administered every 2 or 3 hours, with a total maximum dosage of 120,000 units in 24 hours. Hospitalization of patients treated with penicillin is essential at present since the drug must be freshly made and protected from deterioration, and should be administered by an experienced person.

**Visual impairment during tryparsamide therapy.** William B. Potter. Arch. Ophth., Chicago, 30: 669-687, Nov. 1943.

From a review of the literature on tryparsamide therapy the author has made the following deductions: Although the use of tryparsamide in the treatment of neurosyphilis has been established, an evaluation of the various factors that contribute to impairment of vision during the therapy is not made in the literature. However, it does appear that sex, race or age of the patient are not related to untoward visual effects, nor are the dose of the individual injection, the number of injections, and the length and number of courses of injections associated with visual effects in a consistent manner.

Sloan and Woods have classified the visual effects into two types, the acute and chronic, the latter type being subdivided into objective and subjective. The chronic subjective reaction occurs in approximately 5 to 10 percent of patients receiving tryparsamide therapy and consists of flashes, sparks or spots before the eyes, together with visual distortions and slightly decreased central visual acuity. Objective chronic reactions are found to occur in 4 to 5 percent of patients receiving tryparsamide therapy, with permanent unfavorable results in about 1 percent. This type of reaction consists of contraction of the visual field, involving primarily the upper and lower nasal areas, with relative sparing of the temporal portions. Moderate depression of central vision is frequently noted. The prognosis for restoration of vision is good if the condition is recognized and the drug withdrawn promptly.

During routine administration an initial expansion of the fields with later moderate contraction of the peripheral field has been described as a usual occurrence. Acute reactions are distinct from chronic reactions in all characteristics. Acute reactions usually occur prior to the fifth injection and are characterized by rapid deterioration of both central and peripheral vision.

There seems to be no indication that the presence of optic nerve atrophy contraindicates the use of the drug. When optic nerve atrophy is present there should be a closer surveillance of the patient before and during tryparsamide therapy, with immediate and permanent withdrawal of the drug when there is evidence that there is deterioration of vision from its use.

In the differential diagnosis between the normal condition of the optic disk and that of primary syphilitic optic nerve atrophy, examination of the visual field offers the most thorough information.

The intimate or exact nature of the reaction to tryparsamide remains obscure in the literature. There is no indication that the use of tryparsamide should be condemned; on the contrary, the therapy is fully desirable, but close observation ophthalmologically of the patients is necessary.

**Treatment of chancroid with sulfathiazole. Investigation of the minimal effective dose.** Frank C. Combes, Orlando Canizares and Simeon Landy. Am. J. Syph., Gonorr. & Ven. Dis., St. Louis, 27: 700-702, Nov. 1943.

From their experience with sulfonamides in the treatment of over a thousand cases of chancroid, the authors are of the opinion that protracted treatment is unnecessary since the effect of the drug upon the *Hemophilus ducreyi* is rapid and lethal. After the lesion becomes sterile, continued chemotherapy does not materially influence the healing ulcer.

In a study made of 97 patients with chancroid, 34 were classified as small chancroid, 26 as large, 7 with broken



buboes and 10 with unbroken, and in 20 instances, lesions were artificially induced.

In all the cases, varying amounts of sulfathiazole were administered to observe the clinical and bacteriostatic response. Sulfathiazole was administered as follows: 2 gm. as the initial dose, followed by 1 gm. 4 times daily. A 3-day treatment consisted of 13 gm.; a 5-day of 21 gm.; a 7-day of 29 gm.; a 14-day of 63 gm. All patients were hospitalized and under constant supervision.

The results of the treatment are shown in a table, a study of which shows that the results obtained in the therapy of small and large chancroids during 5 days gave the same results as treatment for 12 days or more. A 3-day schedule was unsatisfactory. In buboes, 7 days of treatment gave the same results as 14 days or more. Experimental chancroids healed more rapidly; in them, 3 days' treatment was always sufficient to control the disease.

From this study the authors conclude that the administration of sulfathiazole for 5 days (21 gm.) in simple chancroid, and for 7 days (29 gm.) if buboes are present, is adequate to cure chancroid. The patient, however, should be closely observed until the lesion is completely healed.

**Toxic effects of arsenical compounds as employed in the treatment of diseases in the United States Navy, 1942.** T. J. Carter, Wesley M. Chambers and Laura T. Anderson. U. S. Nav. M. Bull., Washington, 42: 229-241, Jan. 1944.

In the Navy during 1942 a total of 35 reactions resulted from arsenical treatment. Seventeen of these cases were arsenical dermatitis and were reported in the November 1943 issue of this journal. During 1942, 6,836 persons were treated for syphilis with arsenicals and 5,849 with heavy metal compounds; 1,645 persons were treated with arsenicals for diseases other than syphilis, and 14 with heavy metal compounds. Included in diseases other than syphilis were 5 cases of yaws.

A total of 122,106 doses of arsenicals were given.

Among the patients treated with neoarsphenamine, silver arsphenamine and mapharsen there were 18 reactions other than arsenical dermatitis. Six reactions were classified as of minor importance, 3 as vasomotor phenomena, 2 as liver damage, 2 as gastrointestinal, 1 as Jarisch-Herxheimer, 1 as acute renal damage, 1 as arsenical neuritis, 1 as polyneuritis, and 1 fatal case from blood dyscrasias. In the 6 reactions considered of minor importance, 1 followed the administration of neoarsphenamine and 5 followed mapharsen. In the 3 mild vasomotor reactions, 1 followed neoarsphenamine and 2 mapharsen. Two gastrointestinal, 1 Jarisch-Herxheimer, and 1 renal damage reactions, all mild, followed mapharsen administration. One case of arsenical neuritis followed neoarsphenamine.

The fatal reaction occurred after the administration of silver arsphenamine. In 1932 and 1933 the patient had received 16 injections of arsphenamine and 12 injections of neoarsphenamine. Arsenical treatment was stopped because of a dermatitis. Treatment was resumed in 1941, the patient receiving 6 injections of mapharsen. Fifteen months later the patient was hospitalized and the administration of neoarsphenamine begun. Following his third injection (0.75 gm.) nitritoid reaction occurred. Arsenical medication was stopped but 3 injections of iodobismitol were administered. One month later arsenical therapy was resumed, 0.2 gm. of silver arsphenamine being administered, followed 1 month later by weekly injections of 0.3 gm. Just prior to his seventh injection eczematous purpuric dermatitis appeared on the arm and trunk. Arsenicals were discontinued and in spite of 28 transfusions totaling 9,600 cc. of whole blood, hematuria developed. The patient died 72 days after the onset of symptoms.

The cases with reactions are described in detail.

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## PATHOLOGY

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**Heart disease secondary to syphilitic aortitis.** Ralph H. Fuller and Henry W. Ryder. *Ohio State M. J.*, Columbus, 39: 1126-1128, Dec. 1943.

A previously well 30-year-old Negro woman having exertional dyspnea, orthopnea, and precordial pain was admitted to the hospital. The onset was 5 weeks prior to hospitalization, dyspnea and orthopnea having increased rapidly in intensity, with swelling of the ankles apparent toward the end of the second week. Pain, radiating to either arm, was sharp but not intense, and there were several attacks of syncope the day preceding hospital admission.

Upon physical examination, prominent arterial pulsations were noted and a cardiac apical impulse found in the sixth interspace and in the anterior axillary line. Systolic murmurs were heard at the base and at the apex, and distended neck veins were noted. Neurologic examination did not reveal significant findings. Serologic tests for syphilis were positive. Three electrocardiograms were made.

Under treatment the patient's condition appeared improved, but on the third day a generalized convulsion occurred. An electrocardiogram at this time revealed ventricular tachycardia. In less than an hour another convulsion occurred, and the patient died.

The most common cause of such a syndrome appearing in a young Negro is syphilitic involvement of the aortic valve and coronary ostia. The positive serologic test aids in the differential diagnosis.

Necropsy revealed that the patient had syphilitic aortitis, aortic valvulitis, involvement of the coronary ostia, and diffuse myocardial degeneration, secondary to coronary ostial narrowing. No definitive evidence of a recent myocardial infarction, myocardial gummas, or syphi-

litic myocardial inflammation was elicited.

**Syphilitic angina pectoris.** Evan Jones and D. Evan Bedford. *Brit. Heart J.*, London, 5: 107-120, Apr. 1943.

A series of 103 syphilitic patients subject to paroxysmal pain in the chest has been investigated with special regard to the clinical characteristics of the pain and its pathogenesis.

The age at onset of pain was evenly distributed over the fifth, sixth, and seventh decades, its maximal incidence being actually between 40 and 50 years. There were 80 men and 23 women, giving a sex ratio of 3.5 to 1. A history of syphilitic infection was obtained in 31 cases; the average period between infection and the onset of pain was 24 years. A positive Wasserman reaction was recorded at some stage in 96 cases.

The main clinical findings were aortic incompetence in 67 cases; dilatation of the aorta in 59; cardiac enlargement, often slight, in 83, and essential hypertension in 26. Abnormal cardiograms were recorded in 57 of 94 cases examined.

Seventy-six patients were subject to angina on effort and 64 had pain apart from effort. Nocturnal attacks were common and were usually independent of paroxysmal dyspnea. They tended to be prolonged but were relieved by nitrites. Paradyspneic anginal attacks occurred in 13, a syphilitic status anginosus in 9, and symptoms of coronary thrombosis, not attributed to syphilis, in 10 cases.

Post-mortem findings in 12 cases are given and other pathologic data are considered. The essential lesions of syphilitic angina were found to be aortitis and aortic incompetence, usually combined with stenosis or occlusion of the coronary ostia. Atheromatous and thrombotic coronary occlusion may be coincident with syphilitic aortitis. Pathologic evidence that uncomplicated aortitis causes anginal pain is lacking.

The thesis of an atypical or pseudo-anginal syndrome due to aortitis was examined and rejected. Paroxysmal pain in syphilitic cases conforms to recognized



clinical varieties of angina pectoris such as are encountered in nonsyphilitic coronary and aortic disease. Aortic incompetence and obstruction of the coronary ostia, which affect the blood supply to the whole heart, and cause widespread rather than focal cardiac ischemia, predispose to spontaneous and prolonged pain. The horizontal posture appears to be an important exciting cause of these nocturnal attacks. In paroxysmal pain the effect of posture may be largely mechanical, but in other cases a reflex nervous mechanism may be operative. Consideration of certain cases also suggests that a relationship may exist between pressure pain from a dilated aorta and recumbency.

**Acute dissecting aortic aneurysm: Two cases with an ante-mortem diagnosis in one.** S. L. Zimmerman. *J. Lab. & Clin. Med.*, St. Louis, 28: 1799-1808, Dec. 1943.

The two cases which are reported, together with one other reported in 1936, constitute all the cases of dissecting aortic aneurysm observed in 31,300 admissions in a period of 10 years in the U. S. Veterans' Administration Facility. Among the 360 necropsies during this period these cases give an incidence of 0.84 percent of the autopsied material. These cases occurred in white males 52, 47 and 38 years old.

Hypertension was noticeable in all the patients and the marked variation in the degree of atherosclerosis was striking. The intimal tears in all 3 cases occurred in a portion of the aorta which was relatively free from atherosclerotic changes. The margins of these rents were straight and sharp. None of the vessels showed any of the acceptable criteria for a diagnosis of syphilitic aortitis, the serologic reaction being negative in all three, although a history of inadequately treated syphilis was obtained in one case. All three showed some degree of perivascular round cell infiltration in the adventitia. There was no dilatation of the aortic ring and no separation of the valve commissures. While the presence of a syphilitic

mesaortitis may enhance dissection, Klotz and Simpson have stated that the syphilitic process, being a "granulomatous inflammatory process tends to weld the lamellae more closely together," so that "the wall would split less readily into its anatomic layers."

In the first case the diagnosis was made ante mortem, probably because the patient was hospitalized during the time of dissection and was observed at the probable moment of rupture into the abdomen and pericardial sac.

**Solitary cerebral gumma.** Jack G. Sheps and John L. Simon. *J. Neuropath. & Exper. Neurol.*, Baltimore, 2: 353-364, Oct. 1943.

Solitary cerebral gummas are rare as noted by the fact that only 48 cases of proved cerebral gummas have been reported in the literature. The blood Wassermann reaction was positive in 76 percent and the cerebrospinal fluid Wassermann reaction in 45 percent of these cases. In no case was the cerebrospinal fluid Wassermann positive when the blood reaction was negative.

The authors report 2 cases seen at the Mt. Sinai Hospital. In the first case the clinical features were headaches, mental changes, and focal signs. The picture was ingravescent, suggesting an expanding lesion. Serologic tests pointed to the nature of the disease process, and combined surgical intervention and anti-syphilitic treatment gave satisfactory results. In the second case mental changes, signs of a disseminated cerebral lesion, and a slow pulse were the outstanding clinical features. They led to the diagnosis of an expanding intracranial lesion. The positive blood and cerebrospinal fluid tests indicated syphilis as the etiologic agent.

Gummas of the brain are similar anatomically to those found elsewhere in the body, with the only exception that cerebral gummas tend to break down less frequently. In the 48 cases reported only 1 was reported as breaking down. The glial zone that envelopes a cerebral gumma is not so dense as the fibrous capsule



surrounding a gumma elsewhere in the body.

In the large majority of instances solitary cerebral gummas arise from the meninges over the convexities of the cerebral hemispheres in the region of the central and frontal gyri.

**Experimental infection with *Neisseria gonorrhoeae*. I. Human inoculations.** Justina Hill. *Am. J. Syph., Gonorr. & Ven. Dis., St. Louis*, 27: 733-771, Nov. 1943.

Reports of experimental inoculations of human beings have been published for 175 years. The author has reviewed all such reports that were available and has classified them on the basis of the site of inoculation, subdividing them into studies in which pus or exudates were used for inoculation and in which cultures were employed. The bibliography contains 96 references.

Of the 26 published reports on urethral inoculations with gonorrheal exudates, 18 may be considered as valid. In 23 cases, the inoculations were successful. Of 35 published reports on urethral inoculations with gonococcal cultures, 22 are probably valid and these show that 37 out of 66 inoculations resulted in gonorrheal urethritis. The evidence obtained from an analysis of the reports is in favor of successful inoculations when suitable cultures are placed in normal urethras. The incubation period was sharply defined as 2 days.

The inoculations of glans, prepuce or penis were consistently negative. No experiments have been made with proved gonococci, so that the question of meatal contamination cannot be analyzed. Only 2 of the 7 reports concerning inoculations of female genitalia are of value. Both of these workers used cultures and their inoculations were successful.

Twelve reports on conjunctival inoculations, which include many but poorly described procedures, have been found. Extragenital skin inoculations have been consistently reported negative, except for an occasional abscess formation.

From all these reports, in no case has bacteriologic proof been given either that the organisms used for or recovered after inoculation, were true gonococci. The role of temperature was considered but no rigid conclusions can be drawn from the reports. It is evident that the loss of virulence upon prolonged artificial cultivation varies with different strains and on different media, and that the role of bacterial dissociation might be of extreme importance. There was striking statistical inadequacy concerning the inoculations. However, technics have been described by which gonococcal infections have been obtained by means of artificial inoculations with gonococcal pus or cultures placed in the male urethra, the female urethra, the vagina, the uterus and one in the conjunctivas.

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## LABORATORY RESEARCH

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### **Penicillin as a chemotherapeutic agent.**

Martin H. Dawson, Gladys L. Hobby, Karl Meyer and Eleanor Chaffee. *Ann. Int. Med., Lancaster*, 19: 707-717, Nov. 1943.

Experiments in the use of penicillin as a chemotherapeutic agent against gram-positive organisms and against gonococci and meningococci were begun by the authors in September 1940. Part of their findings have already been reported in the literature.

Penicillin is found to have equally remarkable effects both in vitro and in vivo. Its activity is entirely different from that of any of the sulfonamide compounds, and it has proved of value in sulfonamide-resistant cases. No toxic effects have been found either experimentally in animals or in man, with amounts far beyond the range necessary for therapeutic dosage; in man doses up to 60,000 Oxford units of a highly purified product were given. It is active in the presence of pus and inflammatory exudates. It has proved

effective in man when given intramuscularly, intravenously and intrathecally, its action being either bactericidal or bacteriostatic. It has also proved effective when administered directly into joints and serous cavities as well as in local applications.

Penicillin is rapidly excreted through the kidneys and frequent administration is necessary to maintain an adequate blood concentration.

The small yield and the necessity of supplying material for chemical work has greatly handicapped the clinical use of penicillin. Although the number of cases so far treated is small, this drug promises to be a chemotherapeutic agent of great clinical value.

#### **Easy and accurate method for determination of blood sulfonamides from one drop of blood from the finger tip.**

Johan T. Peters. J. A. M. A., Chicago, 124: 31-33, Jan. 1, 1944.

Because of the necessity for the general practitioner to know the blood level of the sulfonamide with which he is treating a patient, the author has worked out a method by which determination can be made using one drop of blood. This micro-method requires less than half the number of standards used with other reliable methods dependent on Ehrlich's reagent. The stain, which has to be compared with standards, changes much more rapidly in Bratton-Marshall's method than in the methods using Ehrlich's reagent, and this property makes the latter method much more reliable in less trained hands. The method can be performed easily and accurately by the general practitioner.

The procedure is described in full.

#### **A rapid agglutination test technique.**

Nathan Nagle, Lucille Schulze and J. C. Willett. J. Lab. & Clin. Med., St. Louis, 28: 1864-1867, Dec. 1943.

The procedure developed in a rapid agglutination test technic by mixing 0.3 cc. antigen suspension and 0.3 cc. serum dilutions and placing in a Kahn shaking machine for 6 minutes is reported by the

authors from the St. Louis Health Division Laboratories. Preliminary positive results can be reported at once and the final titer can be reported following 5 hours' incubation at 37° C. in a water bath.

Experiments were made on serums of different bacterial diseases, such as typhoid, tularemia and brucellosis, over various periods of shaking and incubation, and it was found that the maximum readings in the majority of the serums were obtained after the 6-minute interval shaking time and the maximum titer developed after 5 hours' incubation.

A close agreement between the results in 36 known positive serums was found by comparing the technic described by the Standard Methods Committee of the American Public Health Association and the rapid agglutination test method. The essential differences between the two methods are shaking and length of incubation period.

#### **Complement fixation test for lymphogranuloma venereum: Results obtained with its use.** Arthur W. Grace and Geoffrey Rake. Arch. Dermat. & Syph., Chicago, 48: 619-625, Dec. 1943.

The authors report their findings of a comparison of the use of the complement fixation test and the Frei test in 130 lymphogranulomatous and 72 nonlymphogranulomatous persons. Positive results were obtained with both tests in 105 persons (52 percent), all of whom either presented manifestations which could be regarded as lymphogranulomatous, or had or had had another venereal disease. In this group of persons, 133 had either a positive complement fixation or a positive Frei reaction or both, 97.7 percent reacting positively to the former and 81.2 percent to the latter. These percentages represent the relative degrees of sensitivity of the two tests.

The serum of a lymphogranulomatous person who yielded a large cutaneous response to the Frei test generally fixed complement in a higher dilution than serum from a person whose cutaneous reaction was small. This suggests either



that the circulating and sessile antibodies are the same or that the concentration of one rises at an equal degree with that of the other. The ratio of the lowest to the highest average titer of serum is much greater than the corresponding figure for the Frei reaction, a fact which should make the complement fixation the more sensitive test of diminution of intensity of infection.

In the group of symptomatic lymphogranulomatous persons, of 34 with proctitis with stricture the serums fixed complement at an average titer of 1:213, with limits of 1:1,920 and 1:6, and of 12 with inguinal adenitis the average titer was 1:98, with limits of 1:480 and 1:6. In 32 persons with neither history nor clinical manifestations of lymphogranuloma venereum the serums fixed complement at an average titer of 1:32, with limits of 1:120 and 1:6.

The authors found that prolonged therapy with sulfonamide compounds in moderate doses did not remove the complement fixing antibodies from the serum of the lymphogranulomatous persons. They believe this is because the infection is not entirely cured but only altered into an inactive, latent form.

**Studies on the detoxication of organic arsenical compounds. IV. The protective action of p-aminobenzoic acid against lethal doses of neoarsphenamine without inhibition of trypanocidal potency.** J. H. Sandground and C. R. Hamilton. *J. Lab. & Clin. Med.*, St. Louis, 28: 1821-1827, Dec. 1943.

Experiments have shown the capacity of p-aminobenzoic acid to protect rats against the "certain lethal dose" ( $LD_{100+}$ ) of various pentavalent arsenical and antimonial compounds. In view of this fact, a large series of experiments have been performed to determine the scope of p-aminobenzoic acid protection in conjunction with several trivalent arsenical and antimonial drugs, such as sodium arsenite, sodium cacodylate, mapharsen, arsphenamine, neoarsphenamine, and tartar emetic.

Three lots of commercial brands of neoarsphenamine were used on a very

heterogeneous assortment of rats. One of these lots (Brand C) had much higher toxicity for rats than the other two. After preliminary toxicity tests with the particular lot of arsenical, protection experiments involving from 5 to 20 rats with an approximately equal number of unprotected controls were usually set up on one or two dosage rates. The assays were often repeated at the same dose rate or with higher or lower doses of neoarsphenamine. The drug was administered in quantities proportional to the rat's weight and rats of various weights were matched equally between treated and control groups. The freshly prepared aqueous solution in 2 to 5 percent concentration was injected either simultaneously with, or not more than 15 minutes after, the administration of a fresh 10 percent aqueous solution of the sodium salt of p-aminobenzoic acid.

In this series of experiments the protective capacity of p-aminobenzoic acid was given its most vigorous test, and appeared to be unequivocally demonstrated, when neoarsphenamine (Brand C) of higher than usual toxicity was employed. Of 120 treated animals, 84 survived, while in 68 control animals only 2 survived. The neoarsphenamine was administered to this group in subcutaneous doses of from 175 to 215 gm. per kilogram of body weight and the p-aminobenzoic acid in doses of 1,000 mg. per kilogram of body weight, either orally or intraperitoneally, to the treated groups. These results show a very substantial reduction in the mortality rate without a concomitant inhibition of its parasitocidal potency as measured by its effect on trypanosomiasis in the rat.

The authors believe that the clinical implication of these findings, especially in connection with the intensive treatment of syphilis, warrant further investigation.

**Viability of *Treponema pallidum* in stored plasma.** F. R. Selbie. *Brit. J. Exper. Path.*, London, 24: 150-152, Aug. 1943.

Three series of experiments have been carried out in which suspensions of rabbit

*Venereal Disease Information, March 1944*



chancre in rabbit plasma have been prepared and their virulence tested after storage at 5° C. for various periods.

In the first experiment, tests were made at intervals up to 48 hours and all samples were virulent. In the second series, tests were made up to 6 days, and virulence was present up to full period of testing. In the third experiment, infected plasma tested for virulence after 6, 10, and 21 days failed to produce lesions in any of the inoculated rabbits. The details of the second experiment are given.

In considering these findings in relation to transfusion syphilis, it must be considered that the numbers of spirochetes in the infected plasma were many times greater than those encountered in human syphilitic blood. Also, the infected plasma was injected, not into the blood stream, but into a sensitive tissue, which largely precluded the operation of the natural defenses of the host.

The risk of transmitting syphilis by blood transfusion would not therefore be so great as the experiments seem to indicate. No transmission of syphilis has been reported from stored plasma. A high proportion of reports of transfusion syphilis has shown that a person related by blood to the recipient was used as the donor.

The fact that *Treponema pallidum* remains virulent for only 6 days under experimental conditions also lessens the possibility of syphilis being transmitted by use of stored plasma.

**Experimental prophylaxis of gonococcal infections.** Frederik B. Bang. *Am. J. Syph., Gonor. & Ven. Dis.*, St. Louis, 27: 716-732, Nov. 1943.

Gonorrhea, from the point of view of the pathologist, should be considered as a superficial infection of certain mucous membranes, rather than as a specific infection of any one structure. Infection of the chorio-allantoic membrane is just such an infection. The experimental infection of the chorio-allantoic membrane of 12-day-old chick embryos with gonococci was used by the author to study the prophylactic value of argyrol, pro-

targol, solutions of sulfonamides, and the arsenicals. This was accomplished by placing the drug directly on the 2- to 3-hour-old membranal infection, removing it 2 minutes later by suction and washing with saline. Controls treated with saline alone remained infected 94 percent of the time.

Argyrol and protargol in water were effective in 50 to 60 percent of the infections. Highly concentrated (10 percent plus) solutions of all the sulfonamides and arsenicals in propylene glycol were effective in more than 90 percent of the infections. The relative value of these drugs determined by the 50 percent endpoint in order of increasing efficiency was: sulfanilamide, sulfaguanidine, sulfathiazole, sulfarsphenamine, "434," mapharsen, neoarsphenamine, clorarsen, and "524." Sulfarsphenamine and sulfathiazole were not clearly differentiated. The four arsenicals—mapharsen, "434," neoarsphenamine, and clorarsen—also had the same order of efficacy. The effect of the drug was influenced by the type of solvent used.

The author says that the available evidence indicated that part of the curative effect was local.

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## PUBLIC HEALTH ADMINISTRATION

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**Venereal diseases and their prevention:**  
Some recent pronouncements. M. J. Australia, Sydney, 2: 299-300, Oct. 9, 1943.

Recently Williams of Canada stated that the roots of the problem of venereal disease lie buried deep in inherent defects of human behavior, in remediable unwholesome community conditions, and a failure to apply effectively the measures of modern medical science. He contended that the responsibility for strengthening the bonds of family life and fortifying individual character lies in the home and the church. The burden of remedying unwholesome community conditions rests on the citizens and on civilian authorities.

He described a "four-sector Canadian front against venereal disease," the sectors including health, welfare, legal, and moral phases of the problem.

At a recent conference, the Archbishop of Canterbury admitted that the church had failed in its duty and he attributed it to the nature of the subject. His ideas of action include: (1) Teaching of the sacredness of sex; (2) making clear the duty and possibility of chastity; (3) providing both in the forces and in civilian life, for abundance of wholesome educational and recreational activity; (4) as far as possible removing inducements to indulge in alcoholic drinks; (5) giving instruction in the dangers inseparable from promiscuity, and in the duty of seeking early treatment if there is the smallest ground for suspecting that infection has been contracted; (6) providing clinics so placed that this early treatment would be facilitated; (7) administering disciplinary action with the suggestion of indignation that any man should have so behaved as to risk the infection.

Many medical authorities agree with the Archbishop's views but point out that many clergy are ignorant on the subject of venereal disease. Ryle states that the medical profession is responsible in that, as teachers of health, they have failed in the education of the laity.

To combat the problem of venereal diseases the general plea is for education, especially of the young. The National Health and Medical Research Council supports this demand in the form of a resolution dealing to a great extent with education. The council contends that, in view of the unusual war conditions, measures are needed that can be applied at once to those who look for guidance and to those who need it but do not look for it.

In a reply to the above article, Haire (*ibid.*, Oct. 23, 1943, pp. 346-347) expresses his disbelief that any organization like the British Medical Association will ever follow the lead which has been given it unless there is a change in public opinion. He also severely criticizes

Weatherhead's book, "The Mastery of Sex," which was recommended to medical practitioners, pointing out many discrepancies in the contents of this book.

**A method of transmitting gonococcus culture specimens through the mail.**  
Daniel Bergsma and Russel Stein. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, 27: 703-710, Nov. 1943.

That culture is superior to spread in detecting the presence of gonococci is known to all investigators. To have this superiority available to general practitioners and scattered clinics is dependent upon a culture service in which specimens can be successfully transmitted by mail. The Bureau of Venereal Disease Control of the State Department of Health of New Jersey has carried out a series of controlled experiments to evaluate the mechanism which a program of this kind would entail.

Specimens were obtained from patients of both sexes at the Newark venereal disease clinic, from treated and untreated patients. Inoculated slants and carrying-tubes were delivered by car to the State Gonococcus Culture Laboratory, approximately  $\frac{1}{2}$  mile from the clinic, reaching the laboratory within 3 hours of the time they were seeded. Spread specimens remained at the clinic for examination. These slants of horse plasma-hemoglobin agar, which were streaked with material obtained from clinic patients, were incubated at 37.5° C. for 18 to 24 hours before being mailed out with return addressed labels. They usually arrived back at the laboratory the following day.

Of 216 positive control cultures, the slant-borne cultures yielded 156 "positives" compared to 71 "positives" reported by spread examinations. Use of the slant-borne technic as a routine laboratory procedure would have yielded 22 false negative reports, whereas 145 false negatives were reported by the spread.

During the latter half of the study, a 26 percent rise in the efficiency of the slant-borne culture method was noted. This would indicate that continued practice



should tend to increase further the reliability of this new technic.

The possible use of this technic as a routine laboratory procedure is being studied further, by means of a State-wide experimental program, and further reports will be made on it.

**The medical profession's responsibility in the prevention of blindness.** Hugo B. C. Riemer. *New England J. Med.*, Boston, 229: 767-769, Nov. 1943.

Medical reports required by the Social Security Board now make it possible to get reliable statistics concerning blindness; it may even be possible to determine the prevalence of blindness from information obtained. In New York, medical forms on file for all blind persons who become known to any public welfare department are cataloged as an aid in initiating studies of any one cause of blindness.

The Division of the Blind of Massachusetts has not received a report of blindness due to ophthalmia neonatorum within the past year. Without doubt this can be attributed to the use of prophylactic drops in the eyes of the newborn, as well as to the premarital and prenatal examination laws.

In a recent study of 1,176 cases of blindness, infectious disease was considered as the cause of blindness in 376 cases (32 percent); 128 cases (11 percent) were due to syphilis, and 51 cases (5 percent) to ophthalmia neonatorum.

A law recently enacted in Massachusetts requires the physician or hospital medical officer to treat the eyes of an infant within 2 hours after birth with a prophylactic remedy furnished or approved by the Department of Public Health, and he must record on the birth certificate the use of such prophylactic. Violators of this section are punishable by a fine of not more than \$100.

The entire medical profession, as well as the ophthalmologist, has responsibility; how well the medical profession car-

ries out the provisions of the laws that aim primarily to prevent blindness will be an important factor.

**A Negro demonstration center for maternal and newborn care in Alabama.** T. M. Boulware, Elizabeth LaForge and R. C. Stewart. *South. M. J.*, Birmingham, 36: 784-791, Dec. 1943.

The Slossfield Maternity Service, in an area densely populated by Negroes, was started through the interest and support of community-minded industrialists, of the State Department of Health, of the Rosenwald Fund, of the Federal Children's Bureau, and of the local white and Negro physicians. This service was instituted in 1940 to develop a teaching center and area for Negro physicians and nurses, to elevate the standards of obstetric and neonatal care, to demonstrate that adequate maternity care will reduce maternal and infant mortality and morbidity. The authors' report was made in May 1943.

During the 3-year period of the authors' study, 308 of the patients who were delivered received antisyphilitic treatment, 154 of whom had positive serologic tests. It is the policy of this center to treat all prenatal patients whose past history reveals a positive serum and treatment, regardless of serologic findings at the time of admission. Approximately one-fourth of all prenatal patients admitted are syphilitic or considered to be syphilitic from their past history. One-third of this group are unmarried.

The types of syphilis seen in these patients were congenital, 1 percent; primary, 2 percent; secondary, 3 percent; early latent, 48 percent; late latent, 39 percent, and undetermined, 7 percent. Sixty-five percent of the patients were considered to have adequate treatment during their current pregnancy. The percentage of living births in this group was satisfactory. Ten arsenic and 10 bismuth injections are considered the minimum of adequate treatment.



# New Cases of Venereal Disease in States, Territories, and Possessions

Health officers' monthly statement: Reported for the first 5 months of fiscal years 1943-44 and 1942-43

Area	Cases of venereal diseases reported for first 5 months of fiscal years below											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital			
1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	
United States†	195,423	234,024	232,520	233,069	252,108	259,632	381,254	3105,781	25,727	26,794	2125,383	2112,572
Alabama	7,236	9,563	1,106	1,189	1,701	2,617	1,774	2,985	172	261	2,963	4,054
Arizona	1,230	726	282	79	327	124	464	488	56	19	725	203
Arkansas	3,809	6,009	502	702	1,281	2,074	1,369	2,499	90	86	2,005	2,131
California	13,198	11,931	2,158	1,656	3,130	2,632	7,220	6,819	411	316	13,488	8,984
Colorado	1,874	1,868	431	347	530	417	841	1,020	72	84	1,409	831
Connecticut	1,296	1,097	150	116	495	272	379	441	67	38	687	653
Delaware	396	372	44	56	92	108	61	120	7	9	75	89
Dist. Columbia	3,456	(*)	442	(*)	847	(*)	1,995	(*)	59	(*)	1,586	(*)
Florida	13,080	13,330	1,370	1,805	3,888	3,034	6,024	6,698	257	304	7,377	5,115
Georgia	7,437	12,642	1,387	1,776	3,062	5,897	2,755	4,611	229	357	4,979	6,320
Idaho	249	185	123	70	48	6	57	80	4	10	368	86
Illinois	11,683	12,600	1,447	1,343	2,822	2,410	7,166	8,532	248	315	9,893	8,909
Indiana	3,775	6,662	531	795	354	83	1,388	2,265	111	204	1,436	1,619
Iowa	1,011	1,192	210	120	254	379	431	557	79	46	784	680
Kansas	1,094	1,652	201	339	224	150	625	710	44	49	860	1,133
Kentucky	3,328	5,797	456	703	737	1,122	1,424	2,445	134	173	1,513	2,023
Louisiana	8,506	8,446	1,277	1,073	2,108	2,300	2,242	4,341	193	278	5,681	2,129
Maine	332	410	72	88	37	60	171	187	30	50	558	299
Maryland	7,271	6,345	710	463	719	513	1,122	724	54	107	3,748	3,388
Massachusetts	2,260	2,388	494	403	0	0	1,647	1,870	119	113	2,104	2,175
Michigan	7,644	5,741	1,052	759	1,963	1,137	3,244	2,480	203	244	4,879	3,959
Minnesota	1,080	1,401	98	89	106	138	797	1,088	51	56	864	664
Mississippi	11,111	17,421	3,823	4,288	3,058	5,945	3,759	6,531	470	657	12,660	13,985
Missouri	4,166	4,776	756	706	1,035	1,001	1,948	2,325	139	138	2,323	1,993
Montana	174	252	50	89	21	16	74	119	4	3	161	127
Nebraska	527	927	87	106	293	204	109	560	19	26	725	762
Nevada	354	362	10	(*)	57	(*)	256	(*)	13	(*)	180	123
New Hampshire	88	134	11	12	28	14	43	87	3	12	83	91
New Jersey	4,906	5,077	581	599	1,571	1,264	2,554	3,024	192	152	2,370	2,969
New Mexico	840	827	187	149	184	147	422	465	47	48	612	241
New York	15,869	15,741	2,358	1,482	2,669	2,620	10,215	11,521	449	533	8,247	7,348
North Carolina	4,757	7,919	1,256	1,673	1,883	3,225	1,527	2,819	91	202	3,873	4,729
North Dakota	137	157	47	23	22	27	49	64	7	11	133	115
Ohio	10,031	10,031	1,461	1,353	2,379	2,300	5,008	5,926	402	452	2,163	2,069
Oklahoma	3,415	4,400	456	645	997	1,548	1,221	1,267	131	121	2,127	1,883
Oregon	898	638	255	105	67	63	552	406	24	47	998	535
Pennsylvania	5,819	2,290	741	514	2,274	1,595	2,151	(*)	299	26	523	(*)
Rhode Island	435	555	30	13	42	46	318	429	10	18	314	170
South Carolina	7,032	8,060	1,459	1,667	2,964	3,233	2,298	2,853	169	212	2,889	2,454
South Dakota	204	204	47	38	31	82	89	67	16	9	179	138
Tennessee	7,835	10,130	1,089	1,223	3,227	3,204	3,266	5,361	167	249	6,914	4,526
Texas	9,563	22,445	1,276	1,385	2,758	4,225	3,595	6,888	258	480	4,566	7,613
Utah	425	248	107	83	61	29	250	128	7	7	272	315
Vermont	120	124	37	70	37	0	42	48	4	6	76	87
Virginia	6,192	8,533	1,893	2,410	2,322	2,958	1,736	2,840	122	177	5,473	3,318
Washington	1,835	(*)	354	(*)	454	(*)	763	(*)	56	(*)	3,568	(*)
West Virginia	1,650	2,395	272	329	224	408	334	674	47	83	1,040	1,072
Wisconsin	420	429	84	76	0	0	332	348	4	5	526	293
Wyoming	666	192	56	60	83	5	312	71	15	1	83	172
Territories and possessions												
Alaska	37	77	24	15	(*)	29	3	20	(*)	5	187	254
Hawaii	354	458	67	156	51	58	216	191	19	20	669	710
Puerto Rico	7,728	4,309	747	914	1,573	674	2,498	1,549	940	760	1,655	1,419
Virgin Islands	91	103	18	29	52	50	15	18	6	6	165	67
Actual total of United States, Territories, possessions†	208,924	238,971	34,182	34,183	55,142	60,443	89,151	107,559	6,820	7,585	133,736	115,022

\*Data not available.

\*\*Includes "Not stated."

†Based on States reporting in both fiscal periods.

‡Includes all reported cases.

1 Based on 47 States.

2 Based on 46 States.

3 Based on 40 States.

# New Cases of Venereal Disease in Cities of 200,000 Population and Over

Health officers' monthly statement: Reported for the first 5 months of fiscal years 1943-44 and 1942-43

City	Cases of venereal diseases reported for first 5 months of fiscal years below											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital			
	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43
Total†.....	1 62,440	1 64,379	2 7,677	2 6,539	3 13,286	3 12,125	3 27,566	3 31,824	4 1,175	4 1,399	1 31,897	1 29,598
Kron.....	406	598	55	93	102	115	230	363	19	27	139	112
Atlanta.....	1,344	1,571	324	469	399	498	609	594	14	10	525	445
Baltimore.....	5,909	4,602	541	317	508	291	858	484	32	29	1,398	1,737
Birmingham.....	2,220	2,856	136	254	615	862	516	692	39	87	272	432
Boston.....	766	886	164	121	0	122	487	573	14	30	578	558
Buffalo.....	830	831	82	67	117	12	609	726	22	26	384	345
Chicago.....	5,898	7,931	936	986	1,457	1,552	3,374	5,179	131	214	5,255	5,952
Cincinnati.....	1,443	1,464	187	142	(*)	(*)	(*)	(*)	(*)	(*)	456	401
Cleveland.....	1,759	1,624	322	276	576	378	818	918	43	52	616	671
Columbus.....	656	616	121	72	133	132	363	394	19	18	135	206
Dallas.....	1,040	1,498	204	166	211	245	616	1,070	9	17	329	539
Dayton.....	871	539	94	86	241	91	506	338	30	20	291	137
Denver.....	899	869	(*)	145	(*)	145	(*)	542	(*)	25	755	433
Detroit.....	5,278	3,403	635	459	1,632	851	2,917	2,018	94	75	2,545	2,150
Honolulu.....	212	290	37	135	33	39	127	101	15	15	486	564
Houston.....	799	1,926	130	157	282	731	356	966	31	72	976	329
Indianapolis.....	(*)	1,831	(*)	284	(*)	52	(*)	521	(*)	18	(*)	328
Jersey City.....	247	323	25	23	50	50	166	240	16	10	20	28
Kansas City.....	774	966	128	136	126	115	487	620	31	44	408	374
Los Angeles.....	4,742	3,660	458	0	1,390	1,330	2,756	2,223	138	107	2,043	2,112
Louisville.....	1,045	1,215	135	135	190	203	445	723	11	22	376	600
Memphis.....	2,777	3,234	250	249	1,330	1,102	1,166	1,837	31	35	2,689	1,050
Milwaukee.....	193	216	24	30	0	0	158	181	1	5	97	59
Minneapolis.....	296	376	50	39	47	61	192	276	5	10	358	292
Newark.....	983	1,180	116	143	255	287	589	731	23	19	396	510
New Orleans.....	(*)	1,840	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	498
New York.....	10,918	11,975	1,900	1,482	2,407	2,140	6,226	7,539	276	307	5,767	5,168
Oakland.....	697	423	80	50	168	97	428	251	15	14	577	340
Oklahoma City.....	1,001	742	99	94	271	245	300	224	15	12	414	335
Omaha.....	239	518	17	54	160	100	47	338	15	15	215	349
Philadelphia.....	(*)	1,388	(*)	162	(*)	3	(*)	1,087	(*)	14	(*)	78
Pittsburgh.....	3,586	3,404	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	23	80
Portland.....	407	323	95	62	27	20	284	221	1	20	407	279
Providence.....	214	264	45	8	13	20	138	211	4	7	69	58
Rochester.....	107	124	20	4	9	1	75	112	3	7	120	89
St. Louis.....	(*)	2,503	(*)	296	(*)	789	(*)	1,339	(*)	79	(*)	638
St. Paul.....	132	232	17	17	24	31	81	169	3	7	139	87
San Antonio.....	503	667	54	68	132	155	297	400	18	34	591	438
San Diego.....	574	439	46	49	167	130	335	254	19	5	392	302
San Francisco.....	1,236	1,461	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	885	1,347
Seattle.....	568	571	67	63	112	68	353	403	9	4	689	562
Syracuse.....	451	278	14	11	17	1	406	259	14	7	130	47
Toledo.....	420	284	69	22	85	50	251	196	15	16	52	81
Washington, D. C.....	3,456	(*)	442	(*)	847	(*)	1,995	(*)	59	(*)	1,586	(*)
Actual total‡.....	65,896	71,941	8,119	7,426	14,133	13,114	29,561	35,313	1,234	1,535	33,483	31,140

\*Data not available for all or part of period.

\*\*Includes "Not stated."

†Based on cities reporting in both fiscal periods.

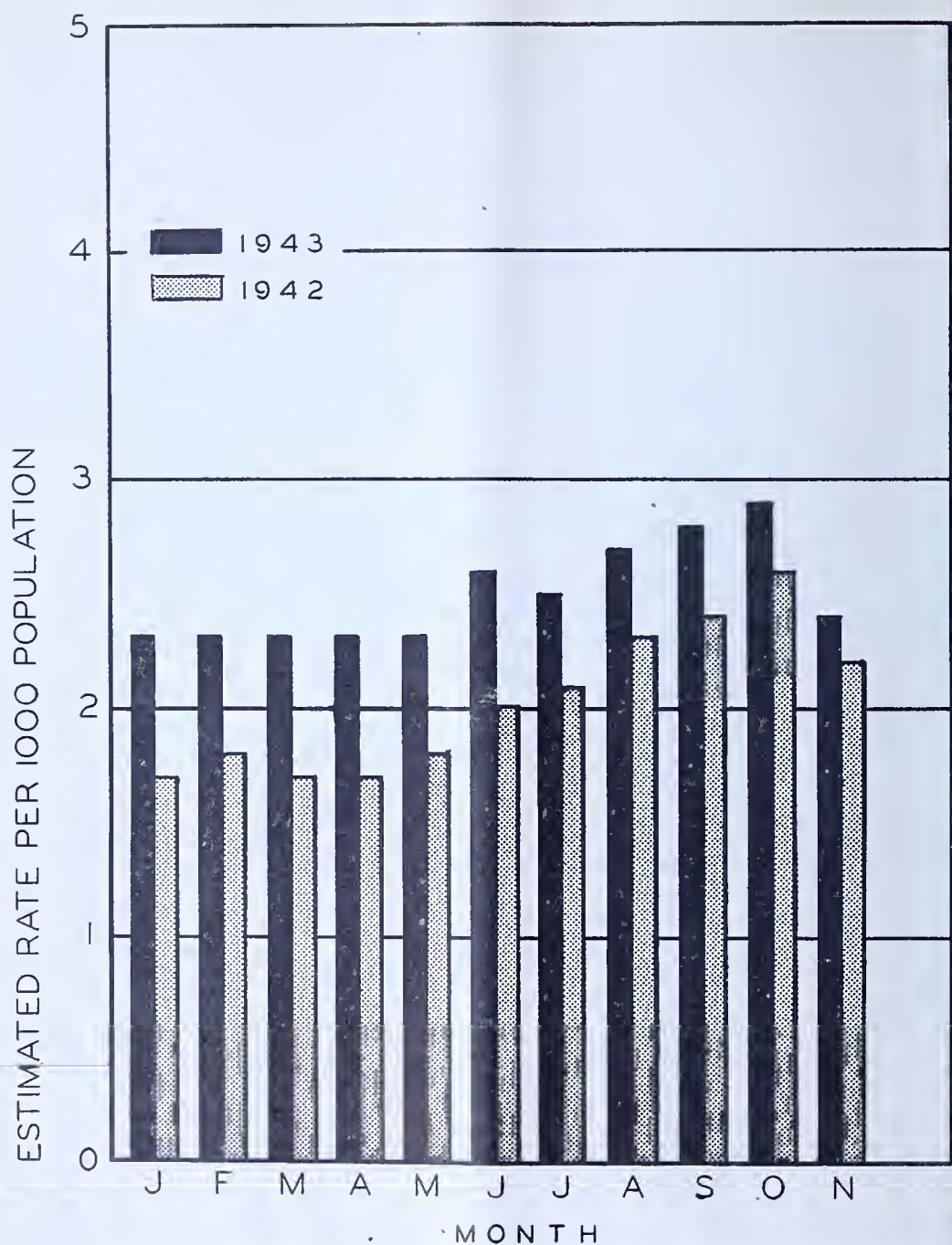
‡Includes all reported cases.

1 Based on 40 cities.

2 Based on 37 cities.

3 Based on 36 cities.

4 Based on 35 cities.



ANNUAL GONORRHEA CASE RATES  
IN THE UNITED STATES  
BASED ON PROVISIONAL MONTHLY DATA  
1943 AND 1942



# Venereal Disease Information

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FEDERAL SECURITY AGENCY  
UNITED STATES PUBLIC HEALTH SERVICE

THOMAS PARRAN, *Surgeon General*

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*Chief, Venereal Disease Division*

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# The One-Day Treatment of Syphilis With Fever and Mapharsen

Nathaniel Jones, Passed Assistant Surgeon (R),<sup>1</sup> Charles M. Carpenter, M. D.,<sup>2</sup> Ruth A. Boak, M. D.,<sup>2</sup> Stafford L. Warren, M. D.,<sup>2</sup> and Henry Hanson, M. D.<sup>3</sup>

Several forms of intensive therapy for syphilis are under investigation at the present time. It is recognized that a method for the rapid treatment of the disease, equally as safe as the standard type of therapy, would have the advantages of shortening the stage of infectivity, eliminating a long period of treatment, and decreasing the cost of therapy.

Investigations during the past 15 years have shown that although physically induced fever is effective in the treatment of general paresis (1), it is of little value in early syphilis (2). Because of the failure of induced fever to cure primary and secondary syphilis in man, a study employing subcurative doses of arsenical compounds concurrently with fever was carried out on experimental syphilis in rabbits.

The first observations indicated that favorable results were obtained from a single intravenous injection of neoarsphenamine (10 mg. per kilogram of body weight) followed by a 3-hour fever at 41.5° C. (3). Later experiments with various combinations of fever and mapharsen demonstrated that the most effective method consisted of a single intravenous injection of mapharsen in the amount of 2 mg. per kilogram of body weight at the termination of a fever at 41.5° C. for 3 hours. The success of this type of therapy in experi-

mental syphilis in rabbits suggested that it might be of value in human syphilis.

The present report records the preliminary results in the treatment of early syphilis with fever and mapharsen. It is based on observations made through Sept. 1, 1943. The work is being carried on at a center established for the rapid treatment of venereal diseases at the Duval County Hospital, Jacksonville, Fla.

## SELECTION OF PATIENT

Patients selected for the study are limited to those with clinical evidence of early syphilis who have had no previous antisyphilitic treatment. The diagnosis is verified by darkfield and serologic examinations. Contraindications to this type of therapy are active pulmonary tuberculosis, heart disease, class II and class III, active renal disease, peripheral vascular disease of any type, and extreme obesity. The majority of the patients treated were young adults: 79 percent were Negro, 21 percent, white; 46 percent, male and 54 percent, female.

## EXAMINATION AND PREPARATION OF PATIENT

The patient is admitted to the hospital on the afternoon of the day prior to treatment and given a general physical examination. A chest roentgenogram and an electrocardiogram are made whenever indicated. A urinalysis and a test for hemoglobin are the only laboratory examinations carried out routinely. Before treatment, the patient is given approximately 3,000 ml. of water, and a total of 12 gm. of sodium chloride in 4-gm. doses at approximately

This study is being carried out in cooperation with the Division of Venereal Diseases, U. S. Public Health Service.

<sup>1</sup> U. S. Public Health Service.

<sup>2</sup> The Departments of Bacteriology and Radiology, The University of Rochester School of Medicine and Dentistry, Rochester, N. Y.

<sup>3</sup> Commissioner of Health, Florida State Board of Health, Jacksonville, Fla.



4-hour intervals. No special dietary precautions are observed. Breakfast is permitted on the day of treatment.

#### TREATMENT

The treatment consists of the concurrent use of fever and mapharsen. The amount of drug and the time of administration in relation to the fever are based on results obtained in the treatment of experimental syphilis in rabbits with a similar type of therapy. Because animal experiments have shown that fever increases the toxicity of mapharsen, subcurative amounts of the drug were employed for the treatment of the first series of patients to avoid toxic reactions. Three schedules of treatment have been used.

*Administration of mapharsen.*—The three schedules are:

Schedule A: Mapharsen in the amount of 1 mg. per kilogram of body weight is administered during the period of induction of the fever, but before the temperature reaches 39.5° C. (103° F.). The calculated amount of drug is dissolved in sterile, triply distilled water and injected intravenously.

Schedule B: Mapharsen in the amount of 1 mg. per kilogram of body weight is injected intravenously in the evening, and fever therapy is carried out the following day. A second intravenous injection of 1.5 mg. of mapharsen per kilogram of body weight is given at the termination of the fever. The calculated amounts of the drug are dissolved in sterile, triply distilled water and injected intravenously.

Schedule C: Mapharsen in the amount of 2 mg. per kilogram of body weight is administered at the termination of the fever. The drug is dissolved in distilled water as in the other schedules. It is then added to 250 ml. of 5 percent glucose in a 0.85 percent solution of sodium chloride and injected intravenously by the drip method. This procedure requires about 15 minutes and is usually completed by the time the temperature has receded to 40.5° C. (105° F.).

*Fever therapy.*—At 7:30 a. m. on the day of treatment, the patient is placed in a Rochester Radiant Energy Cabine (4). The specific gravity of the blood plasma is used as a guide to insure a normal fluid balance during fever (5). The temperature is gradually elevated to 41.1° C. (106° F.) during a period of 2 hours and is maintained at that temperature for 5 hours. The rectal temperature is recorded continuously by means of a resistance thermometer and is also checked periodically with a clinical thermometer. At 10-minute intervals pulse rate, respiratory rate, and temperature are recorded. During the fever the patient is given from 300 to 400 ml. of fluid per hour by mouth when the specific gravity of the plasma is low (1.0258 or less), and from 400 to 600 ml. per hour when high (1.0288 or higher). Throughout treatment the patient is under the constant supervision of a nurse especially trained for this type of therapy.

At the termination of the 5-hour fever the cabinet is opened to permit defervescence, which usually requires about 1 hour. The patient is transferred to bed and the temperature observed hourly until three normal readings (37° C. or 98.6° F.) have been recorded. No restrictions are placed on the patient other than rest in bed for several hours. The majority of patients are discharged from the hospital on the morning following the day of treatment, although a few leave in the evening after treatment.

*Observations made on patients after treatment.*—Patients are to be followed for a period of 5 years, returning to the clinic weekly during the first 8 weeks, monthly for the following 6 months, every 3 months during the next year, and annually thereafter. At each follow-up visit observations are made for clinical evidence of syphilis and blood collected for a quantitative Kahn test. Spinal fluid is collected for examination either before the patient leaves the hospital or at the first return visit.

## RESULTS

To date a total of 410 patients has been treated by the method described. Of this number, 280 have had no treatment for syphilis either prior to or following the specified treatment with fever and mapharsen. Seventy-two of these patients, treated according to

schedule A, have been observed for at least 6 months, 34 being under observation for 1 year or longer. One hundred and twenty-two patients, treated as outlined in schedule B, have been followed from 4 to 6 months, and the 86 treated on schedule C have been followed not longer than 4 months.

### *Results of treatment of syphilis with fever and mapharsen*

Treatment schedule	Patients treated	Observation period (months)	Results					
			Relapses				Probable reinfection	
			Clinical		Serologic*			
			Number	Percent	Number	Percent	Number	Percent
1	72	6-12	13	18.1	3	4.2	6	8.3
2	122	4-6	7	5.7	1	0.8	1	0.8
3	86	0-4	2	2.3	0	0	0	0
Total	280		22	7.8	4	1.4	7	2.5

\*No recrudescence of symptoms.

1 1 mg. of mapharsen per kilogram body weight administered during induction of fever.

2 1 mg. of mapharsen per kilogram body weight administered 12 hours prior to fever; 1.5 mg. of mapharsen per kilogram body weight administered at termination of fever.

3 2 mg. of mapharsen per kilogram body weight administered at termination of fever.

Of the 72 cases treated according to schedule A, 13 (18.1 percent) showed clinical relapse, 11 relapses occurring within the first 4 months. Six of the patients were reinfected. The highest percentage of relapses (35 percent) occurred in the group with secondary syphilis.

Of the 122 cases treated according to schedule B and injected with a larger amount of mapharsen, 7 (5.7 percent) have shown clinical relapse to date. There was 1 case of probable reinfection. Again the highest percentage of relapses (21 percent) occurred in the group with secondary syphilis.

Of the 86 cases treated according to schedule C, only 2 (2.3 percent) have shown clinical relapse to date. The longest period of observation is 4 months, however.

The serologic tests for syphilis carried out subsequent to treatment have shown a similar pattern of reversal. A marked decrease in reagin in the blood of patients with primary and secondary

syphilis occurred during the first 2 months after therapy. Thereafter, the disappearance of reagin was much less rapid. In the case of patients treated for early latent syphilis, the positive serologic test was reversed more slowly than in early syphilis. The blood tests for syphilis on approximately 30 percent of the patients, observed from 4 months to 1 year, have become negative. Quantitative Kahn tests on the blood of the remaining group still show from 4 to 20 units of reagin depending on the time elapsing between treatment and observation of the patient. A serologic relapse has occurred in only 4 patients, 3 on schedule A and 1 on schedule B.

## DISCUSSION

The preliminary results obtained from the concurrent use of fever and mapharsen indicate that this mode of therapy compares favorably with other recently described forms of intensive therapy for early syphilis. The results



on man have paralleled those obtained in the treatment of experimental syphilis in rabbits. Certain modifications in the procedure were necessary, however. Patients were given a 5-hour fever at 41.1° C. (106° F.) instead of a 3-hour fever at 41.5° C. (106.7° F.) as given to rabbits.

Experiments on rabbits carried out in our laboratory have shown that fever enhances the toxicity of arsenical compounds (6). Our observations on patients have paralleled these findings and indicate that fever practically doubles the toxicity of mapharsen. This result is in contrast to that described by Rose, Simpson and Kendell (7), who, in a preliminary report on the treatment of human syphilis with fever and arsenicals, stated that fever decreased the toxicity of the drug.

The patients treated by the methods described showed no evidence of a nephritis, which was reported by Thomas, Wexler, Schur and Goldring (8) to occur subsequent to the concurrent use of fever and arsenicals. It should be pointed out, however, that the total dose of mapharsen which these investigators administered to their patients was far in excess of the amount employed in the procedure heretofore described.

With the type of treatment outlined in schedule A, 8 percent of the patients showed evidence of medical shock and 15 percent exhibited gastrointestinal symptoms such as nausea, vomiting, and diarrhea. Shock did not occur among patients treated according to schedule B, but 8 percent complained of mild headache and vertigo. The gastrointestinal symptoms were exhibited in 18 percent of this group and may be attributed to the administration of a greater amount of mapharsen. Medical shock was not observed in the patients treated as outlined in schedule C. Gastrointestinal symptoms occurred only occasionally, and a few patients complained of headache and vertigo. Because schedule C produces the least discomfort to the patient and seems, so far,

to be at least equally effective, the use of schedules A and B has been discontinued.

The majority of relapses, both clinical and serologic, occurred during the first 3 months after treatment, most of them developing in patients with secondary syphilis. The cases listed as reinfections met the criteria of possible reinfection as set forth by Stokes, Cole, Moore, O'Leary, Parran and Wile (9). Relapses are unusual after the first 4 months, but the final outcome cannot be predicted until the end of the 5-year period of observation.

The concurrent use of fever and mapharsen offers a number of advantages. The treatment can be completed within 8 hours, and the entire period of hospitalization averages about 48 hours. Of importance is the fact that the patient is usually able to resume work the day after his discharge. Laboratory tests, such as chemical examinations of blood and liver and kidney function tests, are unnecessary. Under the present arrangement, the cost of treatment is about \$30 per case. Severe complications, such as arsenical dermatitis, hepatitis, encephalopathy or renal damage have not occurred among the cases treated. It was necessary to discontinue treatment in only 4 percent of the cases.

The favorable results, the simplicity of the procedure, and the low cost of treatment indicate that the method has merit. Reports of additional observations on this group and on other patients will be made later.

#### SUMMARY

A method is described for the one-day treatment of syphilis with the concurrent use of fever and mapharsen, employing three different schedules. The most favorable results were obtained when mapharsen in the amount of 2 mg. per kilogram of body weight was administered at the termination of a 5-hour fever of 41.1° C. (106° F.) To date no severe complications have occurred from the use of the procedure.



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# A Study of the Amount of Active Syphilis Found in a Group of Newly Inducted Soldiers

Joe W. Still, Captain,<sup>1</sup> and Eugene Greenwald, Major,<sup>2</sup> Medical Corps, U. S. Army

This study was undertaken during the summer and fall of 1942 because the impression had been gained from venereal disease experience at Fort Belvoir that a number of soldiers were being inducted with active venereal disease, and that their disease was not being discovered at the time of final physical examination. It was felt that if this impression was correct, a study of this nature might point the way toward improved "case-finding" methods in induction centers and might also assist in giving a more nearly accurate estimate of the total amount of venereal disease existing in the young male population.

## METHOD OF STUDY

In order to investigate these questions we undertook a survey of three battalions of soldiers (2 white and 1 Negro) who had been inducted but a few days, at most 3 or 4 weeks, prior to their arrival at Fort Belvoir. These men were all classified 1-A when inducted and presumably were free of venereal diseases. So far as could be determined there was no element of special selection involved; that is, we believe these men were a random sample of men arriving at this post. A graphic summary of the method of study is shown in the accompanying chart.

The first step in the survey consisted in asking each individual the following questions:

1. Have you ever had "bad blood," "buboes," "kernels," "swollen glands,"

"shankers," "pox," "syphilis," or a "hair-cut"? If so, when?

2. Did you receive treatment? If so, from whom?

These questions were asked by non-medical officers, under the direct supervision of a medical officer who assisted them whenever doubt arose.

The next step in the survey consisted of performing blood Kahn tests on the 220 men whose histories suggested previous syphilitic infection. Letters were then sent to the 161 men who named a physician or clinic as having given them previous antisyphilitic treatment; 94 replies were received. Although the information so obtained was often meager, it nevertheless provided us with a much sounder basis for judgment than is available in the 67 cases for which no reply was received, or in the 59 cases in which there was no history of previous treatment.

The third step in the study consisted of: (1) Careful questioning by a medical officer of the entire 220 men whose histories suggested syphilis. (2) Physical examination when indicated, i. e., search for penile scars, lymphadenopathy, and neurologic signs. (3) Examination of spinal fluid in all cases in which the examiner was not certain whether previous syphilis had existed or not. A total of 159 such examinations was made.

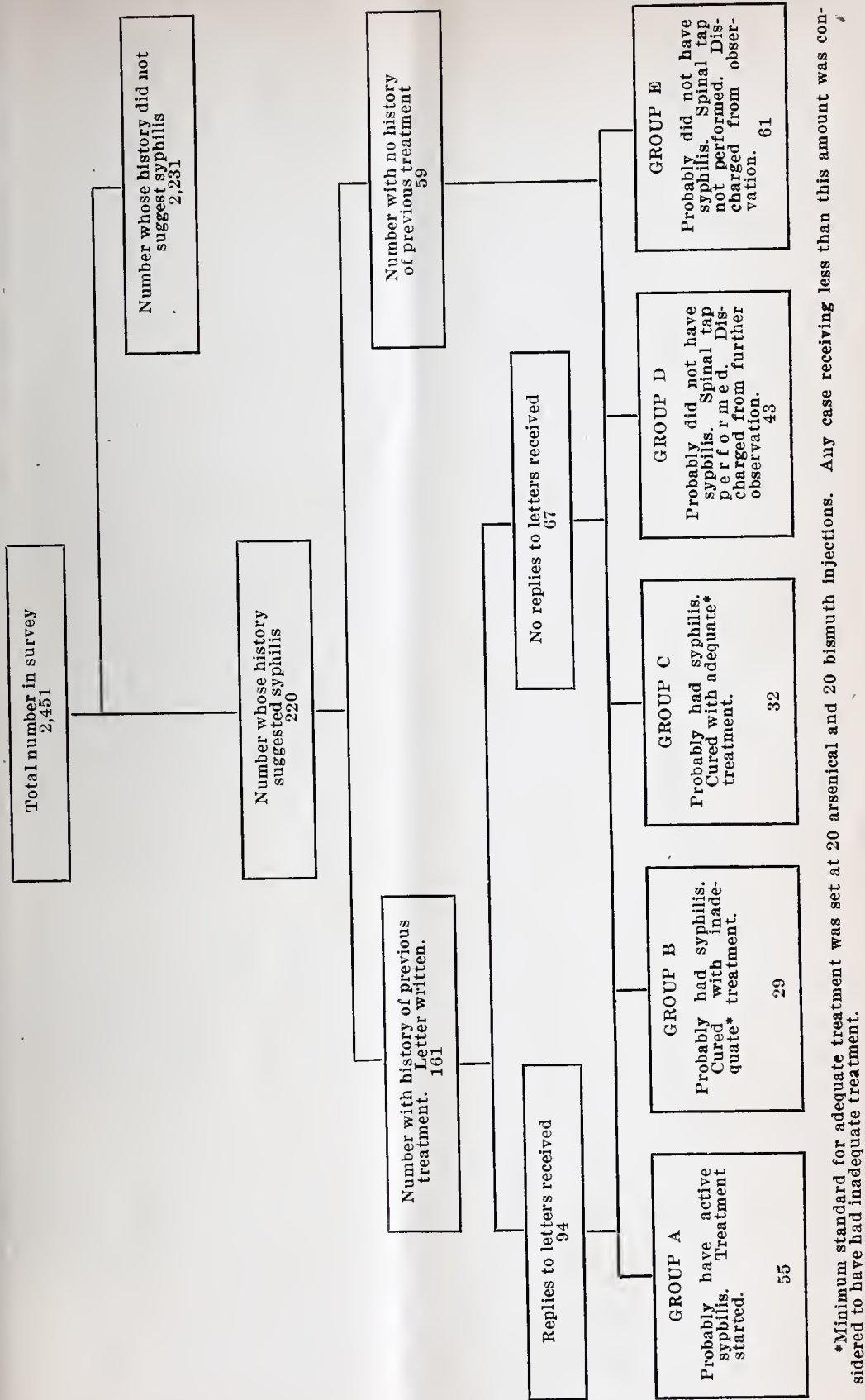
The fourth and final step consisted of sorting the men into the five categories shown in the chart. This, of course, was accomplished on the basis of the information obtained in the described steps.

## RESULTS OF SURVEY

*Group A: Probably have active syphilis.*—Fifty-five men were found to have

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<sup>2</sup> Chief of Genito-Urinary Section, Station Hospital, Fort Belvoir, Va.



\*Minimum standard for adequate treatment was set at 20 arsenical and 20 bismuth injections. Any case receiving less than this amount was considered to have had inadequate treatment.



active syphilis. These were classified as follows:

Diagnosis	Number of cases		Remarks
	White	Negro	
Primary-----	0	3	The chancres in these cases had developed a few days after induction. 2 of them were discovered at the Reception Center before arrival at Fort Belvoir, and 1 was discovered as a result of our survey.
Secondary-----	0	1	This man developed relapsing secondary skin lesions while we were awaiting a reply to our letter.
Neurologic-----	2	6	1 of these men is being discharged from the Army because of meningovascular signs (420 cells/cu.-mm.).
Latent-----	5	38	About half of these cases should be classified as "late" and half as "early."
Total-----	7	48	
Grand total..	55		

The 43 cases classified as latent syphilis fell into one of the following categories:

1. Cases in which the reaction of blood or spinal fluid was doubtful or positive at the time of interview, and in which the history, without medical corroboration, strongly suggested previous syphilis. (No attempt was made to exclude the possibility of false positive serologic reactions due to recent vaccination in these cases, because the histories were highly suggestive of previous syphilis.)

2. Cases in regard to which we had received a statement from a physician or clinic to the effect that treatment for syphilis had been given within 5 years of time of interview and that the total amount of treatment given had consisted of less than 20 arsenical and 20 bismuth injections. The blood and spinal fluid reactions were negative in most of these cases.

3. Cases in which the history strongly suggested syphilis within 5 years of interview and in which treatment had consisted of less than 20 arsenical and 20 bismuth injections, regardless of

serologic findings at time of interview. Most of the men in this group had penile scars or lymphadenopathy to confirm their histories.

*Group B: Probably had syphilis; cured with inadequate treatment.*—In the 26 cases placed in this group the serologic reactions were completely negative and the history strongly suggested syphilis of more than 5 years' duration prior to interview. The men in this group stated that they had received less than 20 arsenical and 20 bismuth injections. In 11 of these cases we received statements from physicians or clinics which confirmed the patient's statement.

*Group C: Probably had syphilis; cured with adequate treatment.*—In 32 cases treatment was considered to have been adequate before induction. The men in this group had been discharged as cured. All had negative findings of blood and spinal fluid, and a history of having received more than 20 arsenical and 20 bismuth injections. Confirmatory statements from physicians or clinics were obtained in 18 of these cases.

*Groups D and E: Probably did not have syphilis; discharged from further observation.*—In the 43 cases in group D there were enough indications of syphilis to warrant an examination of the spinal fluid. When the spinal fluid was found to be negative, the men were discharged from further observation.

The 61 men in group E were discharged from further observation without a spinal fluid examination when questioning and examination by a medical officer failed to reveal any basis for suspecting preexisting syphilis.

The blood Kahn reaction was negative in all cases of both groups.

MISCELLANEOUS RESULTS

*Induction Physical Examination Records (War Department Form 221.)*—We attempted to check our findings in the Negro group with the findings of the induction physical examination. We were able to find a copy of this examination in 69 of the 189 cases in which a search was made.

The 69 Forms 221 which were found showed that 67 men had had one negative serologic reaction and 2 had had one doubtfully positive serologic reaction which was followed by a single negative serologic reaction. In doing our serologic tests, we found 3 positive and 1 doubtful Kahn reactions in men whose serologic reaction was reported as negative on the Form 221.

Each of the 69 forms was examined to see whether any history or findings had been recorded to suggest the presence of venereal disease. History of venereal disease or suggestive physical findings had been reported in only 7 cases, and in no case had a diagnosis of syphilis been made. The notations for these 7 cases were as follows: "No history or sign of syphilis"; "8 anti-syphilitic injections—1940"; "50 anti-syphilitic injections—past year"; "right inguinal scar"; "syphilis with treatment—needs spinal test" (no record that this was performed); for 2, "penile scar" had been recorded. We instituted antisyphilitic treatment in 5 of these cases.

Of the entire group of 69 cases for which a physical examination record was found, we instituted antisyphilitic treatment in 17.

*Replies to letters of inquiry.*—After a lapse of 5 weeks, we had received replies in 94 of the 161 cases in regard to which letters had been sent to local physicians or public clinics requesting information concerning previous treatment. Approximately 25 letters were returned because of "wrong address" or because the named physician had "moved," leaving no forwarding address.

In the cases in which a diagnosis of syphilis had been made previously, the basis for diagnosis usually had consisted of a single positive serologic test. A darkfield examination was reported for only 1 case. It is possible that these findings do not indicate all of the laboratory work which had been performed; consequently, we must be reserved in our criticism of the apparent lack of adequate laboratory findings in these cases.

1. The findings of this study emphasize the great importance of histories as compared with serologic tests and physical examinations in discovering inadequately treated latent syphilis or neurosyphilis. In none of the 51 cases of latent and neurosyphilis which we discovered were the physical findings sufficient to make a diagnosis of syphilis, and in only 10 of these cases was the blood Kahn test either positive or doubtful. In 6 of the cases diagnosed as neurosyphilis, the blood Kahn reaction was negative.

2. The relatively high percentage of responses to our letters of inquiry demonstrates that one can anticipate considerable success in obtaining histories of previous treatment when they are requested.

3. The fact that a few cases in which there had been found an original doubtful or positive serologic reaction followed by a single negative serologic reaction had been dismissed without further study, indicates the need for more careful follow-up work and study. It is just as logical to assume that the negative test was false as to assume that the original doubtful or positive test was false.

4. Since a large number of men who were placed under treatment were cases which lapsed in their treatment at a clinic, it might be advantageous for clinics to notify the military forces, through the medium of United States Public Health Service liaison officers, when lapsed cases are found to have been inducted into service. Many of these soldiers assume that they are cured if they pass their physical examinations, and apparently many civilian clinics are assuming that the induction physical examination discovers these lapsed cases.

5. The fact that a considerable number of men were cured with very inadequate treatment again raises the question of what constitutes "adequate treatment." More detailed study of a larger number of cases similar to those in group B might throw a great deal of light on this complex problem.



# A Multiple-Specimen Container for Mailing Blood Specimens for Serodiagnostic Tests for Syphilis

Charles A. Hunter, Ph. D.<sup>1</sup>

A container for sending a number of blood specimens through the mail has been designed, with the aid of Superintendent of Mails, U. S. Post Office, Topeka, Assistant Postmaster General, Washington, and

edge of the box. The Post Office authorities have stated that there must be  $\frac{3}{4}$ " space between the tubes and the edge of the container. Figure 3 shows a cross

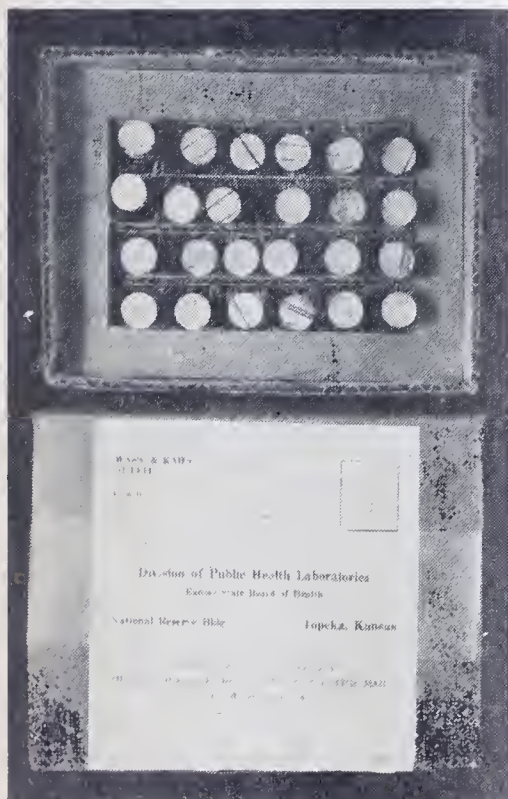


FIGURE 1.

the Jayhawk Paper Co., Lawrence, Kansas. The box is made of corrugated cardboard, 250-pound-test, measures  $7\frac{3}{8}$ " x 6" x  $5\frac{5}{8}$ ", and holds 24 test tubes measuring 4" x  $\frac{1}{2}$ ". Figure 1 is a view of both the top and bottom sections of the box. Figure 2 is a view of the bottom section, with the cardboard liner removed to show the air space between the specimens and

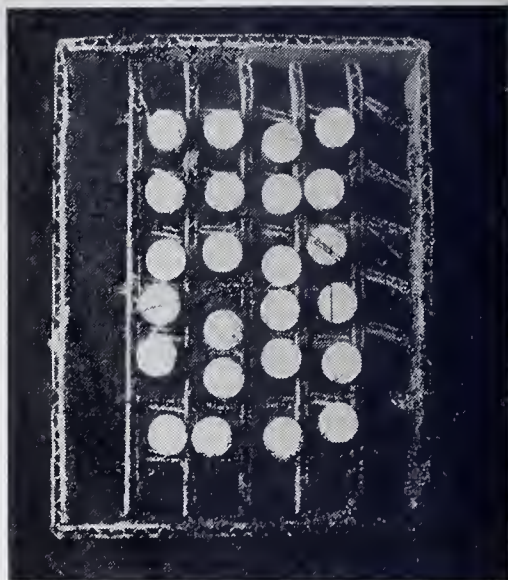


FIGURE 2.

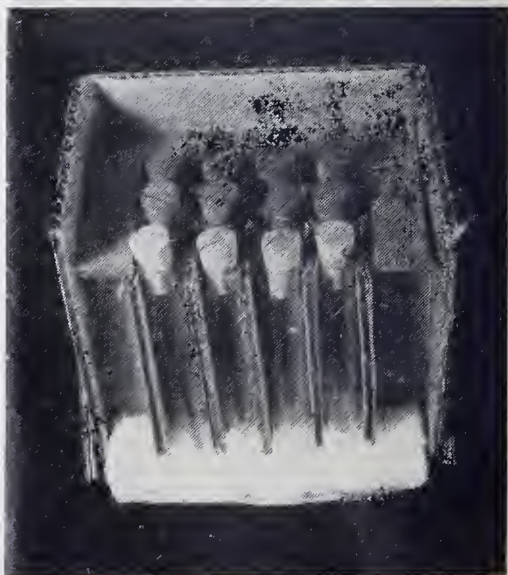


FIGURE 3.

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ection of the lower half of the container, and figure 4 is the cross section of the container when ready to be shipped. It will be noted that when the top half of the container is slipped down over the bottom half, that the container will withstand much weight and abuse, because it has two thicknesses of the 250-pound-test corrugated cardboard. The bottom and top of the container carry pads of cotton, which act as cushions for the tubes.



FIGURE 4.

These containers are inexpensive, being manufactured and delivered for less than 10 cents each. They have been in use for about 6 months and have proved very satisfactory from the standpoint of the laboratory. Selective Service boards, industry, and clinics prefer them to single specimen containers. The local postmasters are pleased with the use of this container since it facilitates the handling of the mail.

## DIAGNOSIS

**"The serology was positive."** Editorial. (J. E. M.) *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, 28: 109, Jan. 1944.

Serology is defined in Webster's dictionary as "the branch of science, especially immunology, treating of the re-

actions, preparation, use, etc. of serums." It is therefore a science, not a test. It is a term which cannot, by definition, be limited to diagnostic tests for syphilis, nor can it be expressed as "positive" or "negative." The misuse of the word "serology" is a solecism which not only the occasional medical author but also experienced syphilographers have perpetrated. The correct expression is "the serologic test was positive."

The author also calls attention to the fact that, properly speaking, the adjective "serologic" is not applicable to spinal fluid tests, since this fluid is not a serum. Scientific accuracy would be better served if, in referring to studies of the spinal fluid, medical writers would name the actual tests employed.

J. E. M. says that he is making a plea "from a weary medical Editor to contributors . . ."

**Intraurethral chancres.** A. B. Loveman and R. P. Morrow, Jr. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, 28: 79-88, Jan. 1944.

During the past 6 months 70 patients with penile chancres were observed at the urologic section of Station Hospital No. 1, Fort Jackson, South Carolina. Eight of these patients (11.4 percent) had endourethral chancres.

The diagnosis of intraurethral chancre is not difficult. The patient usually presents himself at the clinic because of a urethral discharge. This discharge is serosanguineous or seromucoid as contrasted with the thick purulent discharge seen in gonorrhea. Mild symptoms of obstruction to the flow of urine may be present. On physical examination, a painless, diffuse or circumscribed, indurated intraurethral nodule is felt, usually in the anterior portion of the urethra. The final diagnosis depends upon the finding of *Treponema pallidum* by dark field from the discharge or from the regional lymph nodes, if they are sufficiently enlarged to permit this examination.

The 8 cases are reported in detail, together with a description of the diagnostic procedures employed.

**Dark-field examination of material from lymph node puncture: Report of two cases with no evident primary lesions.**

Owen F. Agee. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, 28: 57-58, Jan. 1944.

Various methods are used in the dark-field examination of persons suspected of syphilis. The author has had some success with the darkfield examination of material aspirated from satellite lymph nodes.

Among 124 patients who completed 8 weeks' intensive therapy in the New Orleans Health Department Clinic, all of whom had positive darkfield examinations, there were 6 positive dark fields of inguinal lymph node material. Two of these cases are reported.

The first was the case of a white woman who had a faint generalized follicular rash. There were a few larger papules of the arms, one of which gave a negative darkfield examination. No visible lesions were seen on the external or internal genitalia. The inguinal nodes, particularly the right, were enlarged and rubbery. Darkfield examination of material aspirated from one of the right inguinal nodes was positive for *Treponema pallidum*. Her quantitative Kahn test was 400 units.

The second case was a 14-year-old Negro boy, with a "venereal ulcer of penis, almost healed." Physical examination disclosed redundant mucous membrane of the penis, which had been circumcised in infancy. There was slight firmness near the frenum as evidence of some healed lesion. The inguinal nodes were firm and rubbery. Material from one of the right inguinal nodes was positive for *T. pallidum*. The quantitative Kahn test was 400 units.

In neither case was there history nor evidence of a primary lesion. These cases seem to indicate that node puncture darkfield examination is a useful diagnostic procedure for some undetermined period of time in patients whose satellite nodes persist after the healing of the primary lesion.

The method used was a modified form of Stokes' procedure and is described in detail.

**The value of dark-field examination of lymph nodes in the diagnosis of early syphilis.** A. B. Loveman and R. P. Morrow, Jr. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, 28: 44-56, Jan. 1944.

In a total of 25 cases of early syphilis darkfield examinations of aspirated inguinal lymph node material were performed, and in 23 (92 percent) *Treponema pallidum* was demonstrated. The 2 cases in which no spirochetes were seen were patients with secondary syphilis, one with no evidence of any residual genital lesion, and the other with a chancre which had practically completely involuted.

In 20 cases of the series, darkfield examinations were attempted on either the discharge or local lesion, resulting in 12 (60 percent) negative findings. Thus, by lymph node darkfield examinations an additional 60 percent of the cases were recognized as syphilitic, giving a total of 76 percent of the cases which would not have been accurately diagnosed at the time of admission without the dark-field examination of lymph node material. A local darkfield examination was not attempted in 28 percent of the cases, but the lymph node darkfield examination was positive in all of these cases.

Fifteen nonsyphilitic lymph nodes were examined for spirochetes but all findings were negative. These cases included chancreoid, lymphogranuloma venereum, old healed nonspecific lymphadenopathies, and glands associated with mixed infections.

The darkfield examination of aspirated material from lymph nodes for *T. pallidum* is a practical, accurate, and easily mastered procedure and not infrequently it is the only means of making an immediate diagnosis of early syphilis. The authors give a general discussion of their technic.



### **syphilitic reinfection in a healed tabetic.**

(Die syphilitische Reinfektion bei einem geheilten Tabetiker.) J. Gay Prieto and L. Egea Bueno. *Actas dermo-sif.*, Madrid, 32: No. 2. Abst. in *Wien. med. Wchnschr.*, Vienna, 93: 125, 1943.

A case is reported of a patient who in 1929 had a chancre followed by secondary manifestations, for which he received 3 courses of combined arsenic-bismuth therapy. In 1933 he complained of lancinating pains and vertigo. On examination patellar and Achilles tendon reflexes were absent, the Romberg test positive, blood serum and spinal fluid Wassermann reactions positive, and there was slight ataxia of the lower extremities with definite paresthesias. Following malarial therapy and 3 combined courses of treatment, he was again examined in 1936. At this time there were no subjective disturbances, the Romberg test was negative, serum and spinal fluid Wassermann reactions were negative.

In August 1940 he was again seen, at which time he had, as result of a recent infection, a chancre of the prepuce which was followed by papular secondary lesions associated with strongly positive blood serologic reactions for syphilis. The spinal fluid reactions and the Romberg test were negative. The author based his diagnosis of reinfection on the following: (1) Definite first infection 12 years previously; (2) treatment of the first infection and of the late complications, with disappearance of both clinical and serologic manifestations of the disease; (3) clinical cure of the first infection with sufficiently long interval between first and second infection; (4) second infection with typical primary lesion and secondary symptoms plus positive serologic reactions.

**The so-called exotic syphilis in Annamites of Cochin China.** R. Montel. *Bull. Soc. path. exot.*, Paris, 35: 132-147, Apr. 22-May 13, 1942. Abs. in *Trop. Dis. Bull.*, London, 40: 846-847, Nov. 1943.

The author discusses the old belief that natives of Indo-China, like those of North

Africa, do not have tabes and general paresis, but that due to a special strain of *Spirochaeta pallida* they suffer from syphilis in their skin and skeletal structures. He points out that the severe effects of syphilis on the skin of natives of Cochin China are the result of additional trauma, malnutrition, unhygienic habits, and neglect of treatment. He attributes the apparent absence of cases of tabes and general paresis to the lack of skilled observation. Tabes was overlooked until the ophthalmologists and the neurologists began to examine the native sick more closely, and general paresis victims were usually hidden by their relatives.

From similar observations in China and North Africa, the author concludes that there is only one syphilis, and its effects are largely conditioned by circumstances rather than the make-up of the individual. He does not consider race and climate as influencing factors.

**The incidence and recognition of cardiovascular syphilis.** Benjamin V. White. *Urol. & Cutan. Rev.*, St. Louis, 47: 627-632, Nov. 1943.

Recent statistics compiled by the U. S. Census Bureau, Summary of Vital Statistics, 1943, aid in estimating more accurately the amount of damage produced by cardiovascular syphilis. A geographic computation for 9 census areas, for the District of Columbia, and for the entire United States, of death rates from syphilitic heart disease is shown in a table, classified according to white and Negro population. From the figures for the different areas it is seen that highest incidence was found in the West South Central States, where it was 45.4 per 1,000 population in the white and 307.1 in the Negro population, and the deaths from syphilitic heart disease were 23.4 per 100,000 for the white and 81.5 for the Negro population. The lowest incidence was found in the New England States, where it was 10.7 per 1,000 population for the white and 146.2 for the Negro population, and the death rate from syphilitic heart disease per 100,000 was 5.5 for the white and 38.8



for the Negro population. For the total areas covered by the census the total positive serologic tests per 1,000 population ranged from 109.5 for the East South Central States to 12.2 for the New England States, and the total deaths from syphilitic heart disease per 100,000 population ranged from 34.8 for the South Atlantic States to 6.1 for the New England States. For the entire United States the figures for the two classifications are 47.7 and 17.7, respectively.

From the preventive point of view it is important to recognize and treat syphilis in the early stages rather than cardiovascular syphilis. The recognition of aortic insufficiency or saccular aneurysm is of little importance in the prolongation of life. According to reliable authorities, the expectancy of life in untreated aneurysm and aortic insufficiency averages approximately 2 years after the onset of symptoms; in treated cases the length of life is possibly somewhat greater.

Uncomplicated syphilitic aortitis cannot be recognized by any one diagnostic criterion. The most helpful aid is the 2 meter X-ray film of the chest, but even this is grossly unreliable and may lead to a false sense of security. The recognition of saccular aneurysm and aortic valve involvement may be made by clinical means, but in view of the short expectancy of life after such signs appear, recognition of the disease in this stage adds little to the life expectancy.

**The Migliano reaction for the diagnosis of syphilis. (Use of whole citrated blood and its plasma.)** [A reação de Migliano para o diagnóstico da sífilis. (Pesquisa no sangue total citratado e no seu plasma.)] Luiz Migliano. Bol. san., São Lucas, 5: 51-58, Oct. 1943.

The author presents the results of the Migliano blood test for syphilis used in the examination of 7,787 blood samples. This test showed agreement with the Wassermann reaction in 97.5 percent and with the Kahn and the Kline tests in 98.8 percent of cases.

In addition to these tests, the author examined 1,529 drops of blood by means of his test and found agreement with other types of serologic tests in nearly 100 percent of cases. Either a drop of whole citrated blood or a drop of the respective plasma may be used in this test. If the blood is syphilitic, intense flocculation takes place 1 to 3 minutes after the addition of 2 drops of the author's antigen (the technic of preparing this antigen is not given). It has been found that the blood retains its positive reaction if kept as long as 1½ months after its extraction. Good results were obtained also on dried plasma.

This new test is said to be particularly applicable to the pretransfusion examination of blood.

**The serology in the diagnosis of syphilis with the "Briceño Rossi" reaction.**

(La serologia en el diagnostico de la sífilis con la reaccion "Briceño Rossi.")

A. L. Briceño Rossi. Rev. san. y as. soc., Caracas, 8: 587-598, Aug. 1943.

The author presents the details of the technic of the serologic test for syphilis which he has developed, as follows:

Blood is drawn into a capillary tube and the tube centrifuged at 1,500 r. p. m. for 1 or 2 minutes. The tube is then broken just above the clot and a drop of serum placed on a slide. To this drop, a drop of 10 percent sodium chloride and a drop of Kahn antigen, diluted to a convenient titer 10 minutes previously, are added and mixed. The reaction can be read after 30 seconds.

Strongly positive reactions show large flocculates in a transparent, clear fluid, less strongly positive reactions show smaller flocculates, and 1 plus reactions are characterized by a colloidal suspension of fine particles. In negative reactions there is a homogeneous suspension with no tendency to precipitation nor flocculation.

On a total of 3,072 serum samples this new test compared favorably with the Kahn standard and verification, and with the "Wassermann" tests.

## TREATMENT

**Sulfamerazine.** Wendell H. Hall. Editorial. *Minnesota Med.*, St. Paul, 26: 998-999, Nov. 1943.

Because of its great solubility in water and urine, sulfamerazine has recently been investigated, in the search for a chemotherapeutic agent which might lead to fewer renal complications. Crystalluria and hematuria have frequently occurred in patients treated with sulfadiazine. Effective blood levels can be maintained with smaller doses of sulfamerazine, given at longer intervals, than with sulfadiazine, an initial dose of 4 gm. followed by 1 gm. every 8 hours being sufficient for all except severe infections in adults.

The incidence of crystalluria, hematuria, and blockage of renal tubules, pelvis, and ureters due to sulfonamide crystals does not appear to be any less with sulfamerazine than with sulfadiazine. Maintenance of a urine output of at least 1,200 cc. per day is the most effective means of prevention of renal complications during sulfonamide therapy. From 15 to 20 gm. of sodium bicarbonate per day keeps the urine continuously alkaline.

### **The danger of sulfadiazine in the tropics.**

News and Comment. *Bull. Army Med.*, Carlisle Barracks, No. 70: 1-2, Nov. 1943.

Ravdin and Norfleet warn against the dangers of the use of sulfadiazine in the tropics. Patients under these environmental conditions lose large amounts of fluid through the skin and several hospitals have reported patients with renal complications from the use of sulfadiazine due to low urinary outputs. Most of these cases recover following withdrawal of the drug and the administration of adequate amounts of fluid; some require ureteral and pelvic catheterization and irrigation, or decapsulation. Occasionally death results in spite of all therapy.

The hospital in which Ravdin and Norfleet have been serving has adopted the following precautions: (1) No patient is to receive more than 1 gm. of sulfadiazine every 6 hours except for the initial dose; (2) a careful record of urinary output is charted for all patients receiving sulfadiazine, and a urinary output of less than 1,000 cc. daily is a warning to discontinue the drug; (3) an attempt is made to render the urine alkaline in all patients receiving sulfathiazole and sulfadiazine, and (4) every patient receiving sulfadiazine therapy is reviewed at 24-hour intervals, and the drug is stopped and sulfanilamide substituted as soon as a satisfactory response to treatment has been demonstrated. In this way the therapeutic sulfonamide level can rapidly be attained with a sulfonamide with a wider range of effectiveness, and sulfonamide bacteriostasis continued with a drug of less range of effectiveness but equally less tendency to cause serious complications.

**Sulfonamides: Use of sulfonamides in the Army.** M. G. Flannery. *J. Missouri M. A.*, St. Louis, 41: 28-29, Feb. 1944.

The use of sulfonamides in the treatment of gonorrhea of men in the service has proved of great benefit in decreasing the number of man-hours lost from duty. Formerly from 3 to 6 weeks were necessary to treat these cases with loss of duty for the period of treatment; with the use of the sulfonamides the treatment period has been reduced to 5 days. The treatment is on an ambulatory basis, the men remaining on full duty status. The percentage of cure with the first 5-day treatment is found to be 80 percent. One gram of sulfathiazole is given four times daily for 5 days, followed by 2 days of rest and observation. If tests are still positive, the patient is hospitalized, and another 5 days' treatment is instituted. Local treatment is resorted to if the patient has not responded to the second course of sulfon-



amide, and fever therapy at the end of 20 days if the patient is still not cured.

Frequently after the first day of sulfonamide therapy spreads become negative. This has led to some deception on the part of prostitutes in localities where the health department does routine examinations. When notified to appear for examination they take 4 gm. sulfathiazole the day before, with the result that a negative spread is obtained. In New York the vagrancy law was used to study 375 prostitutes in a hospital for a 10- to 30-day period. The fallacy of treating prostitutes on an ambulatory basis is illustrated by the fact that the minimum number of contacts admitted by any prostitute was 20 per day, and also by the results of the hospital treatment following 10 days of sulfonamide therapy—95 percent were found cured, and after a second course 93 percent.

**The treatment of sulfonamide resistant gonorrhea—preliminary report.** Earl C. Lowry and Linus W. Hewitt. *Mil. Surgeon*, Washington, 93: 449-453, Dec. 1943.

Fifty consecutive cases of sulfonamide resistant gonorrhea were treated at Lawson General Hospital, Atlanta, with fever therapy at 105° F. for 5 hours, after having been given 7 gm. of sulfathiazole during the 18 hours prior to treatment. Eighty-two percent of these cases were considered cured by the first treatment, having met the requirements of (1) no evidence clinically of gonorrheal infection, (2) normal urine, and (3) negative results from 3 prostatic spreads and cultures taken at 4-day intervals following fever therapy. Dispersion of cases following discharge from the hospital has made adequate follow-up impossible.

Since the authors believed that any factors which produced urethral stasis and uncleanness, contributed to chronicity in these cases, phimosis, a small meatus, and urethral strictures were treated before administration of the fever therapy. General supportive meas-

ures such as high caloric bland diet, forcing of fluids to 4,000 cc. daily, hot sitz baths, and absolute cleanliness of the genitalia were considered as important. No severe complications developed as a result of the fever therapy, the most common reactions being herpes labialis, delirium and drowsiness, abdominal cramps, and nausea and vomiting.

Nine cases which were sensitive to sulfathiazole or were failures with fever therapy and sulfathiazole were given fever therapy at 105° F. for 5 hours with 5 to 7 gm. of sulfadiazine. Of the 9 patients thus treated, 7 were cured. The 2 failures were placed immediately on routine urologic treatment.

**The local application of sulfonamide ointments in the treatment of acute gonococcal urethritis in the male.** Oscar F. Cox. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, 28: 66-67, Jan. 1944.

A study to determine the efficacy of sulfanilamide and sulfathiazole in ointment bases applied locally, in cases of early active gonococcal urethritis in the male, was made. Each patient had a purulent urethral discharge in which the gonococcus was detected by spread and culture, and had had no previous sulfonamide treatment for this condition.

Treatment in each instance extended for an exact period of 5 days, 3 to 5 cc. of the ointment being administered locally twice daily. Ointments containing 20 percent and 5 percent sulfanilamide, and 20 percent and 5 percent sulfathiazole were used. During the first 5-day period no other medication was given. Fifty patients were treated by this method. Three (6 percent) of these patients showed a clinical response, all of whom were treated with 20 percent sulfathiazole ointment.

Although the clinical response in these cases was small, the efficacy of the sulfonamide ointments as prophylactic agents is not ruled out if applied locally before gonococci have penetrated the mucous membrane of the urethra.



**Management of the venereal diseases in the Army.** Thomas B. Turner and Thomas H. Sternberg. J. A. M. A., Chicago, 124: 133-137, Jan. 15, 1944.

Recent Army experience in the management of venereal diseases is reviewed. The routine treatment of syphilis has recently been changed to a shortened and intensified scheme consisting of 40 injections of arsenoxide given twice weekly with additional injections of bismuth, covering a total of 26 weeks. The results have been excellent, and from the standpoint of toxic reactions and practicability of administration, the scheme appears to be definitely superior to the older one.

Biologic false positive serologic tests have occurred often enough after vaccination procedures and following acute febrile illnesses to constitute a serious diagnostic problem. Follow-up observations are necessary in order to avoid treating individuals for syphilis in the absence of syphilis.

As a medical problem, gonorrhea is totally different from what it was 5 years ago. Data collected from several stations indicate that over three-fourths of all patients with uncomplicated gonorrhea respond to one or two courses of a sulfonamide drug, that Negro patients respond more favorably than white, and that the toxic reactions from sulfonamide therapy present no serious problem. When patients are treated on an ambulatory basis the end results appear to be nearly as favorable as when treatment is given in a hospital. The authors discuss data which have been collected from four stations, but not published. Urethral instillations, prostatic massage and the passage of sounds are contraindicated in the early phase of the disease for they frequently induce complications.

Penicillin promises materially to change the status of gonorrhea to that of an inconsequential infection; sulfonamide resistant gonorrhea should no longer be a problem, and long continued treatment or fever therapy no longer be necessary.

Among troops stationed in this country chancroidal lesions comprise about 6 percent of all cases of venereal disease. In over 50 percent of such cases there has been a favorable response to therapy with sulfathiazole. The incidence of lymphogranuloma venereum and granuloma inguinale in the Army is relatively low and these diseases have as yet presented no serious problem.

**Penicillin in the treatment of late cutaneous syphilis: Report of a case.** P. A. O'Leary and W. E. Herrell. Proc. Staff Meet. Mayo Clin., Rochester, 19: 20-22, Jan. 12, 1944.

The authors wished to treat a patient who had late syphilis with penicillin. They chose a 42-year-old woman who had had a superficial nodular syphiloderm of the nose for 8 months and who had been treated with local measures only, without improvement. She did not know that she had syphilis, had never been pregnant, and showed no clinical signs of syphilis except the lesion on her nose. Tests on the blood and spinal fluid were positive for syphilis.

Treatment with penicillin was started on Sept. 20, 1943. She was given intravenously by the continuous drip method 20,000 units of penicillin twice a day for 8 days, or a total of 320,000 units, which is about a third the dose required when it is given by the intramuscular route. The patient was hospitalized for the 8 days.

At the close of the treatment the lesion had involuted substantially and 3 weeks after the course of treatment was completed, the slight residual pigmentation was all that remained. The therapeutic result was pronounced in that the lesion healed more rapidly and more completely than is customary after the use of the various arsphenamine preparations in lesions of this type.

One month after completion of the course of penicillin the serologic tests remained essentially unchanged. It is unusual to find a patient with a late syphiloderm and a positive reaction of the spinal fluid, and therefore the au-

thors will continue to observe with interest the influence, if any, of penicillin on the spinal fluid findings. Perhaps in the near future a repetition of the course of penicillin treatment, either intravenously or intrathecally, may be necessary for favorable alteration of the spinal fluid tests.

**Phenarsine hydrochloride in the treatment of syphilis.** William F. Boardman and Robert Kaldeck. *New England J. Med.*, Boston, 230: 12-14, Jan. 6, 1944.

The treatment of syphilis with phenarsine hydrochloride (clorarsen) was begun in the Boston City Hospital 1½ years ago, and the authors report a study of 112 patients. The group included 14 cases of primary, 31 cases of secondary, and 67 cases of late syphilis.

The drug was given in courses of 10 to 20 injections, alternating with courses of 15 injections of bismuth, the doses ranging from 0.030 to 0.045 gm. for women, and 0.030 to 0.067 gm. for men. In the cases of primary and secondary syphilis, 3 injections a week were given for the first 2 or 3 weeks; thereafter weekly injections were given to the end of the first course of arsenicals. In later courses it was administered at weekly intervals throughout. Bismuth subsalicylate in peanut oil was used in weekly doses at 1 cc. (0.075 gm. of bismuth) for 15 doses. Phenarsine and bismuth were never given simultaneously. Cases of late syphilis received a course of bismuth at the beginning of treatment, and pregnant women were treated with phenarsine only.

While there was a fairly high percentage of minor gastrointestinal reactions from the drug when given intensely, in only 7 cases were these so severe that treatment had to be discontinued. Among these, there was one case of liver damage and anemia, but the patient, a 34-year-old female Negro, completely recovered. There were no deaths and no case of clinical nor serologic relapse.

The average time required for healing lesions in primary and secondary syphilis was about 22 days.

The authors feel that the percentage of serologic reversals from positive to negative was as high (32 percent of the 47 cases treated) as that obtained with other arsenicals.

From these findings it appears that phenarsine is a safe drug and further therapeutic investigation is warranted.

**Long-term results in the treatment of latent syphilis.** Thomas H. Discker, E. Gurney Clark and Joseph Earle Moore. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, 28: 1-26, Jan. 1944.

Among 5,326 patients with latent syphilis admitted to the medical clinic of the Johns Hopkins Hospital between 1914 and 1934, there were 926 who had originally normal cerebrospinal fluids, who were observed for 5 years or longer, and who had a complete physical reexamination at the end of this observation period. These cases are a fairly representative sample of the total white group insofar as sex, race, and age are concerned. In the Negro group the proportion of women was significantly higher and that of Negro men lower than in the total group.

Of the 926 patients observed there were 630 (68 percent) who had what was considered satisfactory outcomes, and 239 (25.8 percent) probably satisfactory outcomes. The observed progressions were benign late syphilis 20 (2.2 percent), infectious relapse 3 (0.3 percent), cardiovascular syphilis 20 (2.2 percent), and neurosyphilis 14 (1.5 percent), including asymptomatic 10 (1.1 percent) and symptomatic 4 (0.4 percent). Those patients with positive or negative serologic tests for syphilis who, after 5 years or more of observation, showed no evidence of clinical progression nor relapse on careful physical examination, and whose cerebrospinal fluid, tested at or near the time of the final physical examination, was normal, were considered as satisfactory outcomes. Those in whom there



was an absence of clinical progression but no reexamination of the cerebrospinal fluid were considered as probably satisfactory outcomes. These two groups comprised 93.8 percent of the total number observed.

There were 43 known deaths among these 926 cases from causes other than syphilis.

Women gave a higher proportion of satisfactory results than men, but the differences are within sampling variation. The lowest proportion of satisfactory outcomes was among Negro men; the highest among white women. Cardiovascular syphilis was higher among Negroes and neurosyphilis higher among white persons.

A comparison of the parous and nulliparous women and the men gave no significant difference as to satisfactory outcome.

A study with respect to age at the onset of observation disclosed that neuroprogression was approximately the same in each age group, benign late syphilis appeared predominantly in the age group under 30, and cardiovascular syphilis after 30 years of age.

Although any study of this sort is mitigated by the fact that patients lost from observation cannot be accounted for and that those who are studied represent a random sample of the total group, the authors conclude that their findings strongly indicate (a) that latent syphilitic patients do very well regardless of the type or amount of treatment received and (b) that the optimum amount of treatment to reduce progression to a minimum is approximately 20 injections each of an arsenical and a heavy metal.

**Post-arsenical jaundice and dermatitis:**  
A survey of records from St. Thomas's Hospital, 1929-1941. T. Anwyl-Davies. J. Roy. Nav. M. Serv., London, 29: 153-169, July 1943.

The author is of the opinion that most of the postarsenical reactions are due to decomposition products or to toxic sub-

stances occurring in the manufacture of the organic arsenicals. This is especially true of neoarsphenamine compounds. Additional factors, such as the use of alcohol, starvation, respiratory and renal diseases, may be contributory influences in cases of postarsenical jaundice. The author discusses numerous cases which have been reported in the literature. He also traces the development in 1932 of the trivalent arsenic derivative of arsphenamine, mapharsen, or mapharside as it is called in Great Britain.

For the period 1929-1941, 6,512 male syphilitic patients were admitted to St. Thomas's Hospital. A total of 3,422 patients is analyzed in this report, 2,275 of whom received neoarsphenamines and 1,147 mapharsen. Of the patients who received neoarsphenamine, jaundice developed in 630 (27.43 percent), dermatitis in 160 (6.96 percent), and jaundice and dermatitis in the same case in 22 instances. Of the 1,147 patients who received mapharsen, jaundice developed in 146 (12.73 percent), dermatitis in 14 (1.22 percent), and both conditions occurred in no case.

The shortest average duration of illness from jaundice was seen in patients who received mapharsen (18.7 days per attack).

The use of mapharsen considerably reduced the mortality rate, one death per 20,467 injections occurring during the 5 years, 1936-1940, as compared with 6 deaths in 28,302 injections of neoarsphenamine during the previous 5-year period, 1931-1935, or one death per 5,660 injections. Age and seasonal conditions seemed to have had no effect on the reactions.

The author concludes from his observations in this series of cases that arsenoxide (mapharsen) is a more efficient remedy and is definitely less toxic than the neoarsphenamines. He believes this may be due to the difference in constitution of the drugs and to the method of breakdown either before use or after injection into the body.



**Trial experiments on the use of para-aminobenzoic acid to inhibit toxic reactions in the treatment of neurosyphilis with pentavalent and trivalent arsenicals: Report of failure to prevent secondary reactions.** A. S. Rose, L. D. Trevett, H. C. Solomon and J. H. Sandground. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, 28: 103-108, Jan. 1944.

An attempt is made to determine whether p-aminobenzoic acid would prevent toxic reactions in patients with neurosyphilis given pentavalent arsenical compounds, its value having been demonstrated in animals.

The authors base their experience in the use of p-aminobenzoic acid (paba) in 7 patients. As a whole, the results were not very encouraging. The paba was administered orally, the first dose usually 4 gm. given 1 hour before the arsenical, and subsequent doses of 1 to 2 gm. given at 1- and 4-hour intervals. Tryparsamide was injected intravenously at the rate of 1 gm. per minute and the sodium carbarsone at the rate of 0.5 gm. per minute. In these cases it was found that the administration of paba did not prevent nitritoid crises nor gastrointestinal reaction in the patients treated with tryparsamide nor gastrointestinal reaction in those receiving mapharsen. In one patient given tryparsamide and in another given sodium carbarsone optic nerve reaction was seen. One totally blind patient was given excessive doses of tryparsamide in conjunction with the paba without toxic effects but from their previous experience with this patient the authors doubt whether the drug played a role in making this large dose possible.

**The experimental prophylaxis of chancroid.** Frank C. Combes and Orlando Canizares. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, 28: 59-65, Jan. 1944.

The authors' investigations at Bellevue Hospital were done by autoinoculations of secretion known to contain virulent

organisms obtained from a true chancroid containing *Hemophilus ducreyi*. These inoculations were made on the external aspect of the arm without previous cleansing or antisepsis, using the inoculum from the genital ulcers. The method of multiple puncture, a modification of the Ravaut technic which the authors have found very successful, was used. From 2 to 4 autoinoculations were made on each arm. The prophylactic ointments were rubbed into each inoculation for 2 minutes and then covered with sterile gauze. One control was left on either arm. The time between inoculations and the application of the prophylactic was 1 hour. The incubation period varied from 2 to 4 days. Twenty-eight sets of autoinoculations were made in patients with chancroid and a total of 488 slides from these artificially induced lesions were examined.

It was found that both soft soap and castile soap liniments and calomel and mild mercurial ointments had no prophylactic value. A 10 percent sulfathiazole ointment afforded effective prophylaxis in 80 percent of cases, 5 percent sulfathiazole ointment to a lesser degree, and sulfanilamide powders were ineffective. Sulfathiazole by mouth was shown to be effective but is not recommended for routine use.

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## **PATHOLOGY**

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**Studies in syphilis. IV. The relation between blood serologic tests and anatomic lesions at autopsy.** Bernard Black-Schaffer and Paul D. Rosahn. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, 28: 27-43, Jan. 1944.

The authors continued their study of autopsy reports from the Yale University School of Medicine from 1917 to 1941. They report on a group of 313 syphilitics over 20 years of age, 197 of whom had positive and 116 negative serologic tests on their last hospital admission, and make the following general conclusions:

1. Serologic positivity was significantly more frequently associated with anatomic lesions of syphilis than was serologic negativity.

2. Approximately one-quarter of all syphilitics with specific anatomic lesions at autopsy were serologically negative on their last admission.

3. Approximately one-half of all individuals with positive serologic tests showed no anatomic changes consistent with a diagnosis of syphilis at autopsy.

4. In patients with positive serologic tests, the presence of anatomic lesions was diagnosed correctly in about three-fourths of the cases. About one-fifth of all patients with positive tests as the only indication of infection had organic lesions of syphilis at autopsy, and syphilis was primarily responsible for the death of 1 in 20.

5. In syphilitic individuals with negative serologic tests, a clinical evaluation leading to a specifically stated impression of "no anatomic lesion" or "cured" was likely to be no more accurate when checked with findings at autopsy than a clinical diagnosis of organic disease.

6. About four-fifths of the syphilitics who died primarily as the result of organic syphilitic disease had positive serologic tests. The frequency of positive tests in this group was greater than in the group with anatomic lesions of syphilis an incidental finding at autopsy, while the group with no lesions at autopsy had the lowest proportion of positive tests. This suggests that increasing activity of the disease is associated with an increasing frequency of positive blood tests.

7. Syphilitic organic disease was primarily responsible for the death of about one-quarter of all cases with positive and about one-tenth of those with negative serologic tests. The likelihood of syphilis being the primary cause of death was more than twice as great in individuals with positive as in syphilitics with negative serologic tests.

8. Anatomic changes of syphilis were observed in about one-sixth of those in whom serologic reversal had occurred.

9. Sex did not influence the incidence of positive or negative serologic tests among individuals with syphilitic lesions at autopsy or the frequency of syphilitic lesions as a primary cause of death.

**Thrombosis of the superior cerebral veins as a consequence of meningo-vascular syphilis: Report of case.** Clemson Marsh. Bull. Los Angeles Neurol. Soc., 8: 18-21, Mar. 1943.

The patient, a 50-year-old white woman, presented tabetic crises versus chronic, partial bowel obstruction due to adhesions from previous laparotomies. The pathologic observations at autopsy were not helpful. There did exist a definite degree of vascular syphilis no doubt responsible for the terminal event of phlebothrombosis.

This case was of interest for two reasons: (1) It is not common for a primary occlusion of the superior cerebral veins to be sufficiently extensive in the absence of superior longitudinal sinus thrombosis to produce actual brain damage, and (2) the case demonstrates that syphilitic endo- or periphlebitis is capable of producing a cerebral lesion of sufficient extent to account for the patient's death.

**Dissecting aneurysms.** Lorne Shapiro. Canad. M. A. J., Montreal, 49: 408-414, Nov. 1943.

A total of 7 cases of dissecting aneurysms was seen in 5,380 autopsies at the Montreal General Hospital from 1925 to 1941. Of these 7 cases, 1 had a history of inadequately treated syphilis; this case was that of a 57-year-old man with chronic pulmonary tuberculosis. He had a lung abscess following pneumonia in April 1926. He recovered and felt well until June 19, when pain developed in the right upper abdomen, radiating to the right flank, with spasms of dyspnea and coughing and distress about the heart. Blood pressure was 142/76. A pleuropericardial friction was audible. The patient died on July 1.

Autopsy findings were pericardial sac filled with massive blood clot, the heart



greatly enlarged, and thickening of the cusps of the mitral and aortic valves. Just above the aortic valve was a sclerosed mass, and above this a ruptured area large enough to admit the finger. On microscopic examination the aorta showed considerable atheroma and some small round-cell invasion of the intima and adventitia. This case illustrates the most common site of primary rupture in the ascending aorta, with external rupture into the pericardium. The possible role of syphilis and tuberculosis in damaging the aorta is to be considered; no degeneration of the media was noted.

The other 6 cases are also reported in detail, but in none of them was there mention of syphilis.

In the author's comments on the causation of aneurysms he states that syphilitic mesaortitis is unusual since absence of frank syphilitic disease of the aorta is generally regarded as one of the outstanding differences between ordinary aneurysm and dissecting aneurysm. In well developed syphilitic aortitis with fibrous replacement and interruptions crossing the laminae of the media there is a tendency to localize the sac and prevent extension, but in some cases dissection is extensive. In this connection, syphilis may weaken the wall by toxic necrosis of the muscularis in the infiltration or adventitial changes.

**Syphilis of the stomach.** Felix Cunha.  
Urol. & Cutan. Rev., St. Louis, 48:  
32-39, Jan. 1944.

From available literature, personal study and observations, the author has drawn certain conclusions regarding the diagnosis and treatment of syphilis of the stomach. He says that a positive Wassermann reaction in a patient with a roentgenologically demonstrable gastric deformity places the burden of proof on keen and relatively fast analysis of all the factors present, bearing in mind that there is no reason why a syphilitic cannot also have a malignancy, and that a

benign ulcer can occur in a syphilitic person.

In arriving at a correct diagnosis certain subjective and objective findings have been found to have the utmost significance: (1) An unduly long history of illness. (2) The presence at most of a moderate anemia only—no cachexia or jaundice. (3) The presence of normal free acid values or even hyperchlorhydria as obtained by gastric analysis. (4) The absence of blood in both gastric content and stool. (5) A combination of extensive tissue involvement as seen by X-ray with relatively good general appearance of the patient.

In order to prevent a possible operative mortality and surgical chagrin, it is the 'duty of clinicians and surgeons to take every means possible to insure correctness of diagnosis. An attempted resection of a syphilitic gastric lesion can only result in much grief to both patient and surgeon.

The histories of 3 of the 9 cases which have come under the author's observation are given.

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## LABORATORY RESEARCH

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**Penicillin assay: Outline of four-hour turbidimetric method.** D. A. Joslyn.  
Science, Lancaster, 99: 21-22, Jan. 7, 1944.

The author describes in detail a method of determining the potency of penicillin solutions which, he says, is advantageous in that it is conveniently set up and makes possible the turbidimetric reading of the test in the same test tubes in which the culture is grown. In these respects it is believed to be more practical than turbidimetric methods proposed by others.



**Studies on the absorption of penicillin from the stomach.** Charles H. Rammelkamp and John D. Helm, Jr. *Proc. Soc. Exper. Biol. & Med., Utica*, 54: 324-327, Dec. 1943.

Further studies were made on the absorption of penicillin from the gastrointestinal tract. The standard solution of sodium salt of penicillin dissolved in 0.85 percent sodium chloride in a concentration of 1,000 Oxford units per cc. was used by the authors in their experiments.

As a result of the authors' observations, it seemed likely that destruction by the acid of the gastric juice was responsible for the apparent poor absorption of penicillin when administered by mouth. This suggests that the drug should be absorbed when given by mouth to patients with achlorhydria. In 2 patients with pernicious anemia the concentration obtained in the serum and the amount excreted in the urine showed that penicillin was absorbed readily, even greater than observed in normal subjects. It was found that saliva, bile, and succus entericus did not inactivate penicillin, which suggested that oral administration of penicillin might be accomplished effectively by the administration of large amounts of alkali.

**Darkfield diagnosis of penile lesions: Differential motility characteristics of *Treponema pallidum*.** Reuben Cares. *J. Lab. & Clin. Med., St. Louis*, 29: 82-90, Jan. 1944.

The author had the opportunity of studying early penile lesions at the Station Hospital, Camp Cooke, California. Out of 100 consecutive cases examined in a 6 months' period, 14 were positive for *Treponema pallidum*, the darkfield findings being corroborated by Kahn and Wassermann tests. Among the 20 penile lesions found positive for spirochetes, 14 were positive for *T. pallidum*, 6 for *B. refringens*, 3 for *Sp. phagedenis*, 1 for

Vincent's spirochetes. Infection with 2 species occurred 3 times, twice with *pallidum*, and once with 2 nonspecific spirochetes.

The darkfield features of *T. pallidum* are described in detail. The motility forms of *T. pallidum* are discussed in two main groups. One group, the motility of locomotion, is considered under rotation or propulsion. The rotation type of locomotion may be moderately rapid on an imaginary longitudinal axis of the spiral or it may be sluggish or leisurely, being most rapid in early lesions. The propulsion type implies forward or backward axial motility of the length of the spiral, with little removal of the spiral from one spatial point to another. The spirochete has only a stately and unhurried travel, is never fitful nor spasmodic in its motion.

The other group, the motility of change in shape, is considered under angulation, buckling, coil compression, coil expansion, looping, and undulation. Of these six types of change in shape, angulation is designated as a diagnostic motion of the pallida. Buckling resembles a coil spring being forcibly compressed by end pressure. This is almost as frequent a behavior as angulation and is most characteristic of the pallida. Undulation is best described as the long axis of the organism undulating or fluctuating about a central fulcrum in a manner similar to that of a magnetic compass needle on its center bearing, and it is most apparent when the organism is in the stage of rest. The compression and the expansion of the coils are independent of each other; compression may or may not precede expansion. In the latter the increase in length of the organism is approximately one-fourth. In looping, the whole loop may slowly rotate on a transverse diameter, like a ring transfixed on a rotating pole.

**Decrease of prothrombin concentration in massive arsenotherapy: A preliminary report.** Frederick Kalz and Lea C. Steeves. *Am. J. Syph., Gonor. & Ven. Dis., St. Louis*, 28: 89-95, Jan. 1944.

The authors carried out various laboratory studies at the Royal Victoria Hospital in the hope of finding functional changes which might indicate an imminent danger of hemorrhagic encephalitis in massive arsenotherapy.

In this report the prothrombin time was determined before, during, and after treatment in 15 patients, 8 in the primary stage and 6 in the early secondary stage of syphilis, and 1 an infant with congenital syphilis. In 10 of these cases mapharsen was given in 1,200 mg. dose over a 5-day period and in 3 a corresponding dose of clorarsen (phenarsine hydrochloride) was given. A 2-year-old child with acquired syphilis in the secondary stage and the congenitally syphilitic infant received a total of 50 mg. mapharsen per kilogram by intravenous drip over the 5-day period. All patients were on a diet high in carbohydrate, low in fat, with added vitamins B and C.

The one-stage rapid bedside method of Smith was used to determine the prothrombin time in adults and the simplified microprothrombin technic of Russell and Page in the children. A reduction of the prothrombin concentration occurred in all cases, reaching a maximum on the fifth day. The findings in these cases are illustrated in graphs. The 5-month-old infant with congenital syphilis was the only fatality seen and was the only case in which the prothrombin reduction progressed significantly after termination of treatment.

In the discussion, the authors state that although it cannot be presumed from their observations that hypoprothrombinemia constitutes one of the precipitating factors in encephalitis, it can be concluded that the reduction of the prothrombin concentration indicates a toxic effect of the arsenical on the liver. It seems likely that the detoxifying or conjugating faculty of this organ may be

impaired simultaneously, thus facilitating arsenical toxic effects on capillaries and other tissues. Further investigations will be made in this field.

The question of whether massive arsenotherapy may not cause lasting minor damage to liver function is raised. Whether the hypoprothrombinemia could be prevented by concurrent medication with vitamin K or liver extract, or both is a further problem.

**The relative importance of certain factors in the low-temperature preservation of malaria parasites.** Reginald E. Manwell and Ruth Edgett. *Am. J. Trop. Med., Baltimore*, 23: 551-556 Sept. 1943.

The senior author has already reported studies pertaining to the low-temperature preservation of malaria plasmodia, and in this investigation the authors attempted to clear up some of the doubtful factors of the work. A large number of tests to determine the relative importance of the thickness of the container, freezing temperature, storage temperature, time of storage, and mode of rotation on the viability of malaria parasites after freezing and thawing have justified the following conclusions:

Thin glass tubes are better than thicker ones. Those found best in this work were of Pyrex glass, and measured 100 x 10 mm., varying between 0.018 and 0.030 inch in thickness.

The temperatures at which freezing is actually done seem to be much less important than the storage temperature. It has been possible to preserve plasmodia in viable condition after freezing at a temperature as high as  $-10^{\circ}$  C.

The temperature of the refrigerated container must remain reasonably low; just how low for best results is still uncertain. But plasmodia will not remain viable for even 24 hours in the ice compartment of an ordinary electric refrigerator when set at the minimum (about  $-10^{\circ}$  C.).

If kept in the dry ice cabinet, malaria plasmodia will remain viable for periods at least as long as 244 days, and prob-



ably for much longer. So far no evidence has been obtained to indicate gradual deterioration ("progressive death") of the frozen parasites.

Mechanical rotation is very much more effective than manual rotation during the freezing and thawing process, and gives much more consistent results.

**The prevention of renal precipitation of sulfadiazine in dogs.** Ole J. Jensen. *Am. J. M. Sc., Philadelphia*, 206: 746-756, Dec. 1943.

The effect of pH on the solubility of sulfadiazine has been studied by in vitro and in vivo experiments. It was found that insoluble sulfadiazine becomes relatively soluble as salt formation is induced by raising the urinary pH. Experiments in dogs showed that when the pH of the urine exceeds 7, crystalluria is minimal, higher urinary concentrations of drug are obtained, and the total quantity of drug excreted is likewise higher. The converse was true during acid therapy, when the urinary pH was below 7. The pH and sulfadiazine levels in the urine specimens of dogs under therapy gave a curve closely simulating the in vitro solubility curve.

The subcutaneous administration of sulfadiazine increased the degree of absorption so that smaller doses had to be used.

It has thus been shown that the raising of the urinary pH above 7 increases the solubility of sulfadiazine and prevents its precipitation in the kidneys of dogs. This increased solubility of the drug in alkaline solutions suggests a method of treatment of renal obstruction resulting from the precipitation of the sulfonamides. In the ureteral and pelvic lavage therapy of sulfonamide renal obstruction, alkaline bicarbonate or carbonate solutions are recommended, since these will dissolve drug crystals much better than warm water or normal saline solution. These methods of prophylaxis and treatment are under clinical trial.

## **Gasanalytic and electronoptic studies of the mode of action of the sulfonamides.**

(Gasanalytische und elektronenoptische Untersuchungen zur Wirkungsweise der Sulfanilamide.) Vonkennel, Kimmig and Lembke. *Deutsche med. Wchnschr., Leipzig*, 69: 129-130, Feb. 12, 1943.

The numerous positive results obtained in the respiration thermostat with exactly controlled temperature and experimental conditions are proof, according to the authors, of the direct effect of sulfonamides on gram-negative bacteria. It was found that various sulfonamides were still highly active in dilutions of 1:100,000, some even in dilutions up to 1:1,000,000, not only against gonococci but also *B. coli* and the related paratyphoid bacilli.

The effect of the sulfonamides on bacterial metabolism can be demonstrated by decreased oxidation and decreased gas formation. Electronoptic photographs of gonococci show that sulfonamides cause morphologically detectable changes in the bacterial cells. Before the sulfonamide is added to the culture the bacterial cells are dense, homogeneous, but after the drug has been added they are less dense, less homogeneous, appear mottled and show beginning disintegration. (Three photographs are shown.)

**The fate of the virus of lymphogranuloma venereum in infected mice receiving sulfonamide therapy.** Enid C. Rodaniche. *J. Infect. Dis., Chicago*, 73: 173-179, Nov.-Dec. 1943.

With few exceptions, virus diseases have proved very resistant to chemotherapy; it has been found that the administration of sulfonamide compounds has aided in treatment of clinical and experimental lymphogranuloma venereum infections. The author has conducted experiments to determine some of the results in drug-treated animals.



Groups of mice injected intracerebrally with lymphogranuloma venereum virus were maintained on a diet containing 1 or 2 percent of powdered sulfadiazine or sulfathiazole. At given intervals mice from each group were killed, their brains pooled and the virus titer determined by inoculation of normal mice. The results showed that there was considerable loss of virus from the brains of mice within a few hours of intracerebral injection, and this loss was no greater in treated than in untreated animals. At the end of 7 days there might be a small decline in the virus titer of the brains of the untreated mice, but there was a marked decline in the treated animals. Although the concentration of virus tended to be less in treated animals, there was no loss of virulence.

The spleen was used for a study of the fate of the virus in an extraneural focus. Virus was not recovered from the spleens in the large majority of treated animals, although it was readily isolated from the spleens of treated animals.

Experiments were conducted to study the inhibition of para-aminobenzoic acid upon the therapeutic action of sulfathiazole, and it was found to exert some antagonistic action against sulfathiazole in this viral infection.

By other experiments it was found that lymphogranuloma virus did not become resistant to sulfonamide therapy within 7 mouse passages.

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## PUBLIC HEALTH ADMINISTRATION

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### The management of venereal contacts.

James H. Lade. Health News, Albany, 20: 207-208, Dec. 13, 1943.

The Attorney General of New York, in a communication dated Nov. 17, 1943, renders the opinion that the designation of a woman who had been in sexual contact with a man of the armed services who subsequently developed evidence of

venereal disease is a "reasonable ground" to require her to submit to an examination under Section 343-gg of the Public Health Law. This opinion has clarified a point which has been raised between local health officers and their associates in a few of the up-State cities recently.

The medical corps of the Armed Forces is doing a splendid job in securing the names of persons in the civilian population who have infected service personnel. The proper utilization of this information can accomplish much in the protection of the health not only of the service personnel but also of the civilian population.

It is usually unnecessary to arrest or imprison the recalcitrant individuals, but the threat of such action is an indispensable last resort in the attack of the contact investigator.

**Venereal diseases: Quarantine of infected person "confined or imprisoned in any municipal prison."** *Medicolegal abstracts.* J. A. M. A., Chicago, 124: 124, Jan. 8, 1944.

The petitioner, a woman, was charged with drunkenness and was confined to the county jail under a bond of \$500 for appearance at trial. While so confined she voluntarily submitted to a physical examination, by which she was found to have gonorrhea. The State health officer ordered her quarantined in the county jail pending transfer to one of the State-operated hospitals for the isolation and treatment of persons infected with venereal diseases. The petitioner then brought habeas corpus to secure her release from detention under the quarantine. The trial court denied the petition and the petitioner then appealed to the Supreme Court of Florida. This court affirmed the order of the trial court dismissing the petition for a writ of habeas corpus.

The question presented concerned the validity of the State statute and the rules and regulations of the State board of health under which the petitioner was quarantined, the Supreme Court

said. The constitutional guaranties of personal liberty and private property cannot be unreasonably and arbitrarily invaded, but the preservation of the public health is one of the prime duties resting in the sovereign power of the State. The health of the people has long been recognized as one of the greatest social and economic blessings. The constitutional guaranties do not limit the exercise of the police power of the State to preserve the public health so long as that power is reasonably and fairly exercised and not abused. When such regulations are called in question every reasonable presumption must be indulged not only in favor of the validity of legislative action in this field but also in favor of the validity of the regulations and actions of the health authorities.

While awaiting the decision of the Supreme Court, the petitioner applied for a release on an appearance bond pending the disposition of the appeal; the Supreme Court denied the application without an opinion.

**National conference on wartime problems in venereal disease control.** J. Nat. M. A., New York, 36: 19-20, Jan. 1944.

The American Social Hygiene Association called a meeting in New York on Nov. 22 and 23, 1943, to formulate measures whereby Negro voluntary organizations can cooperate with national health and welfare agencies in the Nation's venereal disease control program. The meetings were under the general chairmanship of Dr. William F. Snow and were attended by leaders in public health work and representatives from both the Army and the Navy.

A general statement approved by the conference as a whole pointed out that because of the war emergency and the military and industrial manpower needs, much attention and service is being directed to the problems of venereal disease control and education for all segments of the population in all sections of the country. "Hence it is considered timely, desirable, and judicious to direct

an adequate share of attention and available personnel and facilities for prevention, treatment, and control of the Negro population, which authoritatively and admittedly has at present a comparatively high rate of venereal disease infection. The Negro should accept the opportunity and assume the responsibility of contributing help from within the race. . . . Obviously the Negro cannot solve this problem alone. It can be solved only by the support and action of the community as a whole."

**The National Venereal-Disease Control Conference.** Editorial. Canad. J. Pub. Health, Toronto, 34: 575-577, Dec. 1943.

A national venereal disease control conference was held in Ottawa in December 1943 for the purpose of considering the venereal disease control program outlined by Lt. Col. Donald H. Williams, Chief of the Division of Venereal Disease Control in the Department of Pensions and National Health, and Army Venereal Disease Control Officer in the Department of National Defense. It was attended by representatives of the armed services, public health workers and organizations in Canada, as well as representatives from the United States, the United Kingdom, and Australia.

The members endorsed the program outlined by Williams for a Nation-wide attack against venereal disease. This program includes the provision of dignified but completely honest and open-minded education of the public; adequate diagnostic and treatment facilities; early, adequate prenatal care, including blood tests; general health examinations, including blood tests before marriage; the suppression of quackery in treatment, and measures to deal with community conditions and persons found to be responsible for the spread of venereal disease.

It was recommended that the Criminal Code be amended to make jail sentences mandatory for men found in houses of prostitution and that heavy penalties be imposed on the owners of property and proprietors of these establishments. A



further amendment to the code was urged to allow the holding in custody of inmates, operators, and those found in houses of prostitution until it is ascertained whether they are free from venereal diseases.

In discussing the incidence of syphilis and gonorrhea, the conference stressed that the public should be given full information concerning the number of cases of venereal diseases in both the civilian population and the armed services. Beginning early in January 1944, the Department of Pensions and National Health will make a survey of the incidence of these diseases in Canada including all public institutions, and will make available weekly data from all parts of Canada.

#### **Medicine's contribution to industry.**

Lemuel C. McGee and Dana D. Burch.  
Delaware State M. J., Wilmington, 15:  
197-201, Nov. 1943.

Among 41,752 preemployment examinations of applicants to the Hercules Powder Company from July 1, 1942 to June 30, 1943, there were 3,623 persons rejected as physically unfit. Of this group, 47 (1.7 percent) were rejected because of syphilitic cardiovascular disease.

The importance of preventive medicine in industry is discussed. Latent syphilis is recognized by means of the preemployment and periodic serologic tests. In 60,619 serologic tests made on workers during the past 2 years there were 1,333 positive findings, an incidence of approximately 22 cases per 1,000 workers in chemical plants distributed over the entire United States. Ninety percent of these persons with latent syphilis did not know of their infection prior to their industrial medical examination. After the diagnosis of syphilis is confirmed, the employees are given antisyphilitic treatment by their personal physicians or clinics. The authors are of the opinion that through this requirement the workers with proved syphilis receive adequate treatment, and numerous instances of subsequent disability from

syphilis of the cardiovascular system, of the central nervous system and of abdominal viscera have been prevented.

#### **Venereal disease education in industry.**

H. Cecil Rhodes and D. E. H. Cleveland. *Canad. J. Pub. Health*, Toronto, 34: 494-501, Nov. 1943.

The Vancouver Junior Board of Trade volunteered its services to the Provincial Board of Health for the development of any phase of venereal disease education considered practicable. As a result, "Industrial Health Education Week" was launched, sponsored by the Junior Board of Trade with the assistance of other associated groups.

A complete mailing list of all firms employing 10 or more employees was compiled. These were divided among the sponsoring groups, whose duty it was to contact these firms and also to check each community to make sure there were no omissions. The results of this campaign are manifold. Although there are no means of measuring the actual benefits, they will produce lasting effects upon their respective communities.

Special mention is made of the work of the groups handling the films, lectures, and literature. The publicity in this campaign included newspaper, radio, billboards, theater trailers, streetcar cards, and window displays. Nearly half a million pieces of literature were distributed and approximately 190,000 employed persons received booklets.

**The antivenereal disease campaign in the Province of Quebec; organization, legislation and social service.** (*La lutte antivénérienne dans la Province de Québec; Organization, législation et service social.*) G. Choquette and E. Lalande. *Union méd. du Canada*, Montreal, 72: 877-880, 1943.

The antivenereal disease campaign had its beginning in the Province of Quebec in 1920 when a Federal division for the control of venereal diseases was created. Appropriations, however, were gradually withdrawn until they were completely stopped in 1931 and the provinces had to depend on their own resources.



A new law for the prevention of venereal diseases was passed in June 1941 according to which anonymous reporting of venereal diseases is obligatory, persons who have contagious venereal diseases must be treated, and the State has the power to interfere when necessary.

At the present time there are 17 dispensaries for the treatment of venereal diseases in Montreal, Quebec, and in 7 other cities of the Province. Free drugs are furnished to these dispensaries by the Ministry of Health, and physicians who treat the indigent patients are compensated by the Ministry of Health.

Educational literature is provided to civilians, soldiers, sailors, and aviators. A medical social service also has been established which is connected with the large clinics in Montreal and Quebec, and with the dispensaries of Lévis, Trois Rivières, and Sherbrooke. In the other dispensaries the Sanitary Units are in charge of social service.

**Public support for the solution of public health problems in Puerto Rico.** R. A. Vonderlehr. Bol. Asoc. méd. de Puerto Rico, San Juan, 35: 469-473, Dec. 1943.

The author gives a vivid account of the health conditions in Puerto Rico and points out the serious need for improvement. The venereal diseases constitute one of the four most serious health problems. For several years the Insular Health Department, aided by funds from the Public Health Service, has waged an intensive campaign on these diseases. This campaign includes provision for the earliest possible diagnosis, treatment with the most efficacious and newest drugs, the follow-up of contacts and delinquent patients, and the teaching of the general public. The need of public cooperation is stressed.

One of the fundamental epidemiologic principles of venereal disease has been totally neglected in Puerto Rico until recent months by allowing segregated or tolerated prostitution.

The need for law-enforcement agencies and the Legislature to take the neces-

sary steps to correct this situation is urgent. The author recommends that the members of the House of Delegates of the Puerto Rico Medical Association adopt the same resolution against prostitution that was adopted by the House of Delegates of the American Medical Association in 1942, namely, that no reputable physician should so degrade his profession and himself as to issue certificates to prostitutes to the effect that they are free from venereal disease.

The proposed Six Year Plan of the Puerto Rico Planning Board seems a comprehensive start toward the attainment of a better health program and deserves the study of every physician and his active support of all those measures that are scientifically sound.

**The syphilis problem in Venezuela.** (El problema de la sífilis en Venezuela.) Juan Iturbe. (Manuscript) Department of Agriculture and Animal Husbandry, Caracas, Venezuela, 1942.

Out of 143,959 serologic tests for syphilis carried out at the National Health Laboratories on blood specimens obtained from men, women, and children during the period 1931 to 1937, and 25,675 tests carried out at the Vargas Hospital on blood specimens sent in from various regions of the Republic during the period 1934 to 1937, a total of 45 percent was positive.

Out of 10,125 Wassermann tests which had been made in the author's laboratory at the time of this report, 26 percent had been found to be positive. Among 475 autopsies carried out at the Vargas Hospital between April 1937 and April 1938 anatomic lesions of syphilis were found in 88 cases (21.8 percent). Syphilis had been the cause of death in 65 of these cases.

From these findings the author concludes that 30 percent of the entire population is infected with syphilis, and that the prevalence of new cases is 15 per 1,000 per year.

The prevalence of gonorrhea is three times greater than that of syphilis.

The author stresses the importance of case reporting and case finding and holding in the control of venereal diseases.

The great prevalence of congenital syphilis is indicated by the findings of Mir, Mora, and Castillo. Among 80 children examined by them 69 (86.2 percent) were found to have clinical and serologic evidence of congenital syphilis. Of 58 children (8 to 10 years of age) whose blood was tested in the author's laboratory, 29 percent had positive serologic reactions for syphilis.

Dr. Pons reviewed 10,000 clinical histories contained in the files of the Vargas Hospital and found that 32 percent of the patients had been hospitalized for syphilis and that 54 percent had positive serologic reactions.

According to the census of 1936, the total population of Venezuela was 3,467,839, of whom 1,109,709 were less than 15 years of age; 1,976,668 between the ages of 15 and 50 years, and 381,462 more than 50 years.

The author estimates that of those under 15 years, 15 percent have syphilis; of those from 15 to 30 years of age, 30 percent.

**Delinquency in the making: Patterns in the development of girl sex delinquency in the city of Seattle with recommendations for a community preventive program.** Mary Louise Webb. *J. Social Hyg.*, New York, 29: 502-510, Nov. 1943.

The need for a concerted program for the prevention of juvenile delinquency is pointed out. Army authorities have reported that a large percentage of infected servicemen have become diseased through contact with amateur sex offenders under 18 years of age. This aggravation of a long-standing problem necessitates an immediate attack by the community, and if such a program is to succeed all persons and organizations directly concerned with the youth of the community

must have adequate knowledge of the causes of delinquency.

Case histories of 40 girl sex offenders, taken from the closed files of the King County Juvenile Court, were used as a basis for study. General cases are discussed in full. They illustrate the emotional conflicts and disturbances engendered in the child in his home situation and the role the school may play in the adjustment of its individual students. The factors uncovered in the process of the study suggest certain recommendations as possible points of concentration in both an immediate and long range program of prevention.

In order that the spread of venereal disease may be checked, that the drift of young women into professional prostitution may be decreased, and that the right to liberty and happiness may be preserved for these young women, it is recommended that the following steps be taken:

(1) The number of truant officers should be increased, in order that serious delinquency may be checked as soon as possible in its development.

(2) The schools should attempt to expand their special programs for students who, by virtue of low intelligence or other handicap, need special attention.

(3) A concerted program aimed at encouraging democracy in the schools should be undertaken, with the abolition of high-school sororities the first step.

(4) Police supervision of the trouble-spots, i. e., the all-night movies, the roller-rinks, the public dance halls, and popular rendezvous, should be widely extended.

(5) An effort should be made even in wartime to prevent mothers of children under 15 from holding more than part-time positions outside the home.

(6) A reasonable program of sex education should be carried out for both high school students and their parents.



*Rapid treatment centers in operation as of February 19, 1944  
(Assisted by Lanham Act funds.)*

Medical officer in charge	Name of hospital	Location
Arizona: Asst. Surgeon (R) R. H. South....	Phoenix V. D. Quarantine Hosp.	205 E. Madison St.
Arkansas: Sr. Surgeon William E. Graham....	U. S. P. H. S. Medical Center....	Hot Springs.
Colorado: P. A. Surgeon (R) W. L. Chadwick.	V. D. Detention Facility.....	Denver General Hospital.
P. A. Surgeon (R) D. W. Dykstra.	Pueblo Rapid Treatment Center..	29th and Court Sts.
District of Columbia: P. A. Surgeon (R) Sidney Olansky.	V. D. Rapid Treatment Center...	Gallinger Hospital.
Florida: P. A. Surgeon (R) George H. Smullen.	Wakulla Rapid Treatment Center No. 1.	Wakulla.
P. A. Surgeon (R) Alexander I. Kernish.	Ocala Rapid Treatment Center No. 2.	Ocala.
P. A. Surgeon (R) Nathaniel Jones.	Jacksonville Rapid Treatment Center No. 4.	Duval County Hospital
Georgia: Sr. Surgeon Austin V. Delbert....	Southeastern Medical Center....	Oatland Island, Route 2, Savannah.
Surgeon (R) Forest C. Hunter....	Augusta Quarantine Hospital....	1 Milledge Rd.
Illinois: Surgeon (R) H. W. Kendell.....	Chicago Intensive Treat. Center...	2449 South Dearborn St.
Indiana: Dr. N. M. Beatty.....	V. D. Isolation Hospital.....	Fletcher Sanitorium, Indianapolis.
Iowa: .....	.....	Des Moines.
.....	St. Joseph Mercy Hospital.....	Sioux City.
.....	University Hospital.....	Iowa City.
Louisiana: P. A. Surgeon (R) Carl C. Kuehn....	Leesville Quarantine Hospital....	Leesville.
Mississippi: P. A. Surgeon (R) Francis D. Wilder.	Public Health Rapid Treatment Center.	Richton.
Asst. Surgeon John F. Flynn.....	do.....	Meridian.
Missouri: Surgeon Leland J. Hanchett.....	St. Louis Rapid Treatment Center..	3630 Marine Drive.
Nebraska: .....	Intensive Treatment Center.....	1702 Grace St., Omaha.
New Mexico: Asst. Surgeon (R) Herbert M. Leavitt.	New Mexico Intensive Treatment Center.	1305 Gold Ave., Albuquerque.
North Carolina: Asst. Surgeon (R) Howard P. Steiger.	Rapid Treatment Center.....	W. 7th and Church Sts., Charlotte.
P. A. Surgeon Evert A. Swensson.	U. S. P. H. S. Medical Center....	P. O. Box 1729, Durham.
Oklahoma: Surgeon (R) Charles A. Shumate...	Okla. State Rapid Treat. Hosp....	Rush Springs.
Panama: Dr. Julio Jimenez S.....	Matias Hernandez Hospital.....	Panama C. Z. H. Dept., Balboa Heights, C. Z.
Puerto Rico: c/o Dr. Juan Lastra Charries.....	V. D. Treatment Center.....	Caguas, P. R.
.....	Aguadilla District Hospital.....	Aguadilla, P. R.
South Carolina: Asst. Surgeon (R) George Fein....	Quarantine Hospital No. 1.....	RFD 3, Box 990, Columbia (Pontiac).
P. A. Surgeon (R) Andrew P. Sackett.	Quarantine Hospital No. 2.....	RFD 2, Box 480, West Columbia.
P. A. Surgeon Clarence A. Smith...	Rapid Treat. Center Hosp. No. 3.	RFD 2, Box 102A, Columbia.
South Dakota: Asst. Surgeon (R) Irving H. Mauss.	.....	Rapid City.
P. A. Surgeon Francis H. Redewill	.....	Sioux Falls.
Tennessee: Asst. Surgeon (R) Edward M. Eckberg.	West Tennessee Isolation Hospital.	Care of Shelby County Hospital, Memphis.
P. A. Surgeon (R) Everett T. Duncan.	Middle Tennessee Isolation Hospital.	Route 6, Box 160, Nashville.
Asst. Surgeon (R) Robert L. Woodard.	Silverdale Isolation Hospital.....	Box 501, Route 2, Chattanooga.
Texas: Asst. Surgeon (R) Vernon L. Hagan.	Quarantine Hospital.....	2627 Louisiana Ave., El Paso.
Asst. Surgeon Chester M. Sidell...	Riverview Hospital.....	102 Dwyer Ave., San Antonio.
Utah: .....	Utah Detention Quarters.....	115 S. State St., Salt Lake City.
Virgin Islands: Dr. Knud Knud-Hansen.....	Municipal Hospital V. D. Annex..	Charlotte Amalie, St. Thomas V. I.
Virginia: Asst. Surgeon Edward W. Kunckel.	Richmond Rapid Treat. Center...	Richmond.
Washington: Asst. Surgeon (R) Fred W. Harb...	Seattle Treatment Center.....	9236 Rerton Ave.
Surgeon (R) Lennert B. Mellott...	Washington Infirmary.....	Grand Mound.



**New Cases of Syphilis and Gonorrhea in States, Territories, and Possessions**  
Health officers' monthly statement: Reported for the first 6 months of fiscal years 1943-44 and 1942-43

Area	Cases of syphilis and gonorrhea reported for first 6 months of fiscal years below											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital			
	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43
United States†	1229, 287	1281, 834	238, 391	240, 940	261, 212	271, 685	396, 108	326, 941	26, 612	28, 018	2147, 857	2134, 802
Alabama-----	8, 739	11, 257	1, 325	1, 416	2, 025	3, 041	2, 051	3, 472	202	295	3, 428	4, 706
Arizona-----	1, 429	946	327	123	388	177	549	589	62	27	869	317
Arkansas-----	4, 412	7, 299	569	823	1, 483	2, 568	1, 589	3, 075	103	105	2, 313	2, 524
California-----	15, 845	15, 120	2, 629	2, 095	3, 745	3, 284	8, 647	8, 694	494	406	16, 510	11, 444
Colorado-----	2, 178	2, 199	508	410	623	498	958	1, 184	89	107	1, 678	1, 060
Connecticut-----	1, 528	1, 410	184	134	614	396	426	535	69	52	804	765
Delaware-----	459	462	56	63	112	119	74	153	8	11	89	98
Dist. Columbia-----	4, 070	(*)	498	(*)	1, 001	(*)	2, 383	(*)	65	(*)	1, 886	(*)
Florida-----	15, 556	17, 010	1, 729	2, 258	4, 769	3, 948	7, 084	8, 546	314	386	8, 966	6, 363
Georgia-----	8, 312	14, 551	1, 589	2, 018	3, 377	6, 719	3, 086	5, 411	256	402	5, 590	6, 843
Idaho-----	294	230	140	83	56	14	75	101	4	12	441	118
Illinois-----	14, 134	15, 075	1, 809	1, 646	3, 336	2, 957	8, 710	10, 096	279	376	11, 916	10, 403
Indiana-----	4, 358	7, 226	632	920	397	141	1, 593	2, 731	126	239	1, 761	2, 282
Iowa-----	1, 195	1, 454	248	151	300	471	513	669	90	51	906	793
Kansas-----	1, 316	1, 999	253	409	272	185	741	834	50	61	1, 008	1, 410
Kentucky-----	3, 777	6, 946	535	820	830	1, 363	1, 619	3, 000	154	215	1, 788	2, 384
Louisiana-----	9, 581	9, 831	1, 519	1, 284	2, 465	2, 731	2, 527	4, 876	218	309	6, 703	2, 821
Maine-----	388	474	83	104	44	71	201	217	33	54	649	348
Maryland-----	8, 273	9, 221	806	635	790	735	1, 289	1, 047	61	121	4, 067	4, 072
Massachusetts-----	2, 820	2, 877	589	483	(§)	(§)	2, 073	2, 253	158	139	2, 581	2, 461
Michigan-----	8, 881	7, 936	1, 267	951	2, 293	1, 438	3, 750	3, 086	227	281	5, 623	4, 846
Minnesota-----	1, 221	1, 608	115	109	125	164	900	1, 243	53	60	976	771
Mississippi-----	13, 080	20, 600	4, 414	5, 052	3, 666	6, 915	4, 481	7, 868	516	765	14, 996	16, 856
Missouri-----	5, 101	5, 536	885	828	1, 321	1, 142	2, 409	2, 684	168	154	2, 813	2, 345
Montana-----	218	284	60	97	41	16	84	136	4	4	178	160
Nehraska-----	670	1, 125	105	125	354	258	161	678	22	33	832	931
Nevada-----	400	412	11	(*)	72	(*)	283	(*)	15	(*)	204	141
New Hampshire-----	113	159	15	16	31	15	57	105	4	14	100	109
New Jersey-----	5, 675	6, 040	666	709	1, 799	1, 514	2, 977	3, 567	225	206	2, 787	3, 566
New Mexico-----	991	971	216	169	223	203	499	530	53	51	744	310
New York-----	19, 101	18, 790	2, 871	1, 730	3, 222	3, 069	12, 245	13, 707	532	658	9, 964	8, 639
North Carolina-----	5, 685	9, 220	1, 492	1, 891	2, 263	3, 703	1, 826	3, 369	104	257	4, 589	5, 480
North Dakota-----	159	188	53	26	26	31	51	79	9	12	149	140
Ohio-----	11, 758	11, 890	1, 773	1, 594	2, 790	2, 723	5, 933	7, 060	481	513	2, 686	2, 390
Oklahoma-----	3, 933	5, 472	508	803	1, 148	2, 049	1, 424	1, 456	148	144	2, 435	2, 253
Oregon-----	1, 020	771	299	132	83	77	606	490	32	55	1, 218	641
Pennsylvania-----	6, 740	2, 819	882	595	2, 638	1, 896	2, 457	(*)	330	31	614	(*)
Rhode Island-----	556	650	42	19	58	53	402	498	12	22	379	218
South Carolina-----	7, 974	10, 151	1, 657	2, 032	3, 269	4, 151	2, 665	3, 590	195	249	3, 403	2, 955
South Dakota-----	254	243	51	45	35	101	121	78	24	10	208	157
Tennessee-----	9, 159	12, 129	1, 234	1, 450	3, 731	3, 885	3, 897	6, 398	201	276	7, 687	5, 137
Texas-----	11, 044	26, 046	1, 454	3, 107	3, 237	4, 856	4, 281	7, 995	284	540	5, 230	9, 244
Utah-----	467	311	120	104	65	34	274	164	8	8	331	390
Vermont-----	134	142	44	76	40	0	45	60	5	6	90	102
Virginia-----	7, 320	10, 031	2, 171	2, 842	2, 772	3, 506	2, 112	3, 322	138	199	6, 346	3, 965
Washington-----	2, 294	(*)	444	(*)	531	(*)	1, 011	(*)	63	(*)	4, 481	(*)
West Virginia-----	1, 848	2, 872	318	386	266	462	390	792	48	95	1, 155	1, 227
Wisconsin-----	485	531	92	105	0	0	389	421	4	6	580	416
Wyoming-----	686	220	57	72	90	6	321	82	15	1	87	201
<i>Territories and possessions</i>												
Alaska-----	43	84	28	18	7	31	4	20	1	5	228	282
Hawaii-----	406	578	71	195	58	67	294	253	22	23	816	817
Puerto Rico-----	8, 550	4, 946	842	1, 042	1, 772	785	2, 788	1, 760	1, 057	873	2, 014	1, 605
Virgin Islands-----	117	118	24	31	69	63	18	18	6	6	196	73
Actual total‡ of United States, territories, possessions-----	244, 767	287, 560	40, 309	42, 226	64, 722	72, 631	105, 346	128, 992	7, 841	8, 925	158, 092	137, 579

\*Data not available for all or part of period.

\*\*Includes "Not Stated."

† Based on States reporting in both fiscal periods.

‡ Includes all reported cases.

§ Included in late and late latent.

1 Based on 47 States.

2 Based on 46 States.

3 Based on 45 States.

# New Cases of Syphilis and Gonorrhea in Cities of 200,000 Population and Over

Health officers' monthly statement: Reported for the first 6 months of the fiscal years 1943-44 and 1942-43

City	Cases of syphilis and gonorrhea reported for first 6 months of fiscal years below											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital			
	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43
Total†.....	1 69,939	1 75,210	2 8,677	2 7,970	3 16,304	3 14,654	3 32,880	3 38,408	3 1,400	3 1,685	1 38,199	1 34,703
Akron.....	461	701	65	102	117	133	256	435	23	31	177	132
Atlanta.....	1,557	1,876	367	509	461	613	712	740	19	14	654	492
Baltimore.....	6,683	7,195	611	468	560	475	984	758	34	39	1,524	2,058
Birmingham.....	2,729	3,563	172	318	713	1,012	583	883	48	92	329	548
Boston.....	895	1,091	178	153	0	147	574	712	22	39	664	639
Buffalo.....	1,021	979	122	93	129	18	744	830	26	38	439	451
Chicago.....	7,602	9,239	1,219	1,196	1,841	1,823	4,388	5,974	154	246	6,620	6,894
Cincinnati.....	1,644	1,821	210	180	(*)	(*)	(*)	(*)	(*)	(*)	507	492
Cleveland.....	2,064	1,922	385	325	653	439	977	1,096	49	62	729	765
Columbus.....	764	764	153	88	161	158	410	494	20	24	159	232
Dallas.....	1,261	1,794	233	217	272	288	746	1,271	10	18	394	617
Dayton.....	990	656	114	102	275	117	570	411	31	22	364	156
Denver.....	1,014	1,126	(*)	178	(*)	184	(*)	721	(*)	28	929	535
Detroit.....	6,093	4,130	762	546	1,881	1,022	3,345	2,470	105	92	2,934	2,530
Honolulu.....	236	377	39	169	36	47	144	143	17	18	577	661
Houston.....	955	2,325	157	182	330	867	436	1,198	32	78	1,150	417
Indianapolis.....	(*)	2,172	(*)	320	(*)	56	(*)	575	(*)	21	(*)	346
Jersey City.....	285	388	26	30	56	63	196	284	17	11	25	31
Kansas City.....	913	1,117	152	166	158	137	566	707	35	50	474	426
Los Angeles.....	5,747	4,319	0	0	2,265	1,544	3,313	2,662	169	123	2,531	2,526
Louisville.....	1,114	1,630	157	169	201	268	472	987	13	38	443	702
Memphis.....	3,309	4,263	289	345	1,563	1,432	1,414	2,412	43	44	2,876	1,137
Milwaukee.....	245	266	29	43	0	0	202	218	1	5	99	72
Minneapolis.....	324	429	52	45	57	70	207	313	6	11	400	338
Newark.....	1,146	1,353	132	164	295	338	685	823	34	28	460	576
New Orleans.....	(*)	2,015	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	551
New York.....	13,206	13,941	2,328	1,730	2,917	2,460	7,476	8,836	336	382	7,135	5,983
Oakland.....	790	587	93	64	190	138	479	350	20	18	691	430
Oklahoma City.....	1,108	957	104	125	308	318	338	298	19	15	475	395
Omaha.....	298	610	22	63	183	121	68	397	18	18	257	434
Philadelphia.....	(*)	1,610	(*)	187	(*)	3	(*)	1,280	(*)	18	(*)	91
Pittsburgh.....	(*)	4,064	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	80
Portland.....	449	393	111	67	29	28	304	271	5	27	490	329
Providence.....	274	301	49	13	21	24	181	238	4	8	87	74
Rochester.....	134	158	26	12	12	1	93	138	3	7	147	108
St. Louis.....	(*)	2,708	(*)	335	(*)	836	(*)	1,455	(*)	82	(*)	697
St. Paul.....	154	270	20	23	27	33	97	198	3	8	158	106
San Antonio.....	590	808	63	70	163	196	344	491	18	38	684	522
San Diego.....	652	590	55	70	184	187	368	324	24	8	452	389
San Francisco.....	1,519	1,885	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	1,084	1,683
Seattle.....	700	677	85	82	130	82	439	469	11	7	851	670
Syracuse.....	521	361	15	12	20	1	471	339	15	9	158	56
Toledo.....	492	348	82	29	96	54	298	248	16	17	72	97
Washington, D. C.....	4,070	(*)	498	(*)	1,001	(*)	2,383	(*)	65	(*)	1,886	(*)
Actual total†.....	74,009	87,779	9,175	8,990	17,305	15,733	35,263	42,439	1,465	1,834	40,085	36,468

\*Data not available.

\*\*Includes "Not stated."

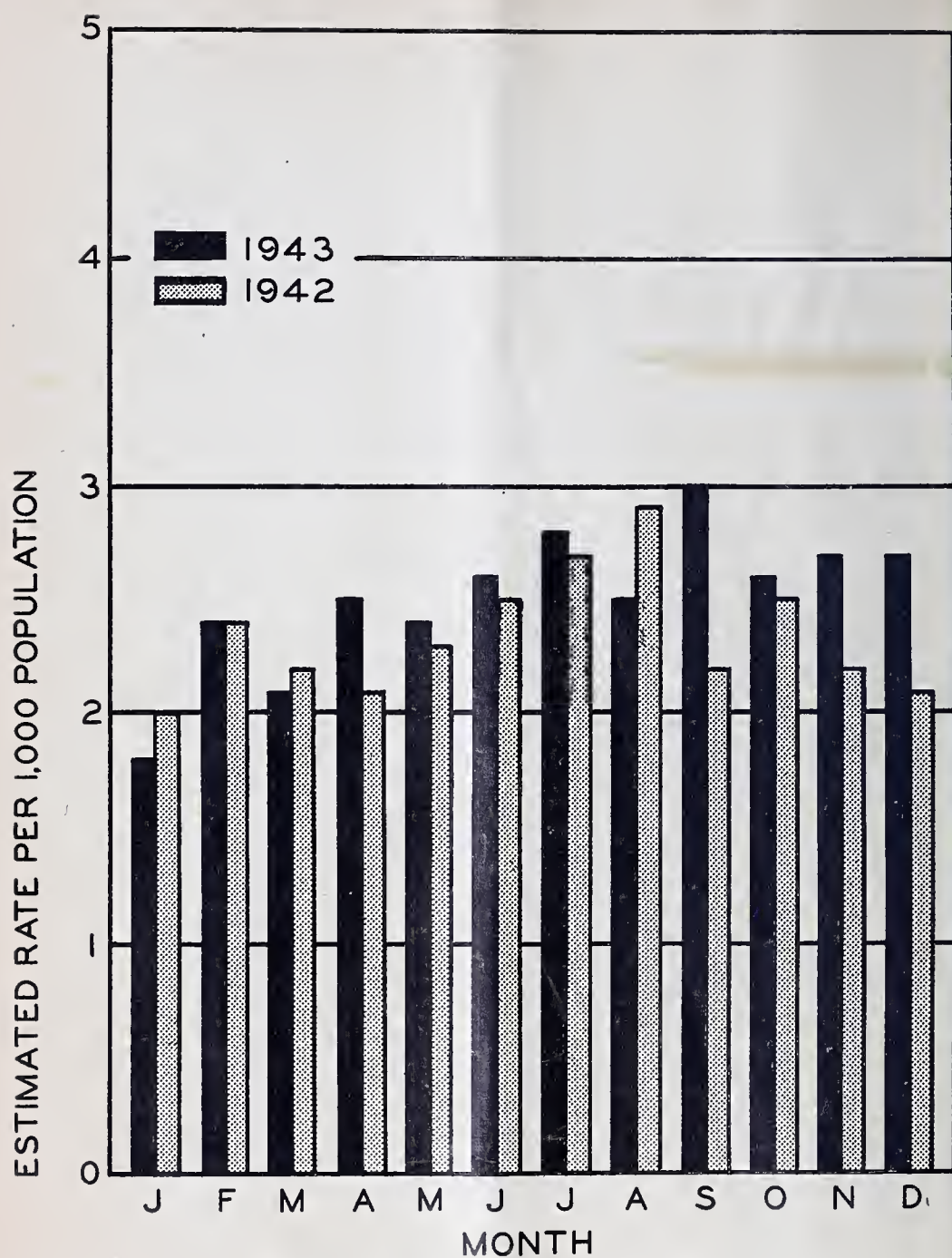
†Based on cities reporting in both fiscal periods.

‡Includes all reported cases.

1 Based on 38 cities.

2 Based on 36 cities.

3 Based on 35 cities.



ANNUAL GONORRHEA CASE RATES  
IN CITIES OF 200,000 POPULATION AND OVER  
BASED ON PROVISIONAL MONTHLY DATA  
1943 AND 1942





# Venereal Disease Information

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G. H. FAGET, *Senior Surgeon*  
SISTER HILARY ROSS, B. S.

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# Evaluation of Positive Kolmer and Kahn Tests in Leprosy

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The significance of positive serologic reactions in leprosy has long been a point of contention among physicians treating the disease. While at present most leprologists agree that a positive complement fixation or flocculation reaction occurs in leprosy in the absence of syphilis, there are still a few who do not agree with this. The latter argue that the frequency of positive serologic reactions in leprosy can be accounted for by the prevalence of syphilis and yaws in these patients. The literature on the subject will not be reviewed here, since it has already been fully and aptly covered by Cooke (1), Hasseltine (2), Badger (3), and others.

The true meaning of a positive complement fixation test for syphilis in leprosy is certainly not realized by the general practitioner in the United States. If it were, over one-third of the patients admitted to the National Leprosarium would not have been subjected to active and at times extensive antisymphilitic therapy before the diagnosis of leprosy was confirmed. The general practitioner should learn that leprosy is one of the diseases most apt to give a false positive complement fixation test and that this test is of no value in the differential diagnosis of leprosy from syphilis. Not only the general physician but the dermatologist and syphilologist as well should be familiar with this fact.

Two very enlightening serologic surveys were conducted by the United States Public Health Service in 1935 and 1942 (4, 5). Both demonstrated that leprosy produces false positive complement fixation and flocculation reactions for syphilis. The first survey included 13 different complement fixation and flocculation

tests for syphilis, which were carried out on, among others, 50 blood specimens of presumably nonsymphilitic leprosy patients of the National Leprosarium. Positive results varied from 40 to 76 percent, with an average of 59 percent for all the tests on leprosy patients. The second serologic survey included 28 separate complement fixation and flocculation tests for syphilis which were performed on 60 blood specimens of presumably nonsymphilitic patients of the National Leprosarium. Positive reports varied from 14 to 70 percent, with an average of 45 percent positive.

Not only are positive serologic tests common in leprosy, but during the course of the disease it is not unusual for changes to occur in these tests. These changes in serologic reaction are observed to parallel closely the changes in the clinical manifestations of the disease. With improvement, a positive test tends to become negative, and with aggravation of the disease, it often changes from negative to positive. The purpose of this paper is to add further evidence in confirmation of this fact, which was pointed out by Badger (3) in 1931. This fluctuation in the serologic reaction in leprosy, which accompanies exacerbations and remissions in the disease, is strong evidence in favor of the presence in leprosy serum of an antibody capable of reacting with the antigens of the various syphilis tests.

## PRESENT OBSERVATION

The clinical records of all new patients admitted to the National Leprosarium since July 1, 1928, were carefully reviewed. Subsequent to that date the Kolmer complement fixation and the Kahn precipitation tests were adopted as routine laboratory procedures on all new admissions. Experience had shown that among numerous serologic tests assayed,

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they were the most specific (gave the least number of false positive reactions) in leprosy. This has since been confirmed by further studies of various serologic tests at the National Leprosarium, the Mazzini slide test being the only possible exception. In this paper, only Kolmer and Kahn tests will be taken into consideration.

Table 1 gives the results of Kolmer and Kahn tests performed on new patients admitted since July 1928. All tests were done by the same laboratory technician. It demonstrates the frequency of positive blood serologic reactions, particularly in lepromatous and mixed leprosy, and explains why these patients are so often mistakenly treated for syphilis.

TABLE 1.—Positive Kolmer and Kahn tests among 695 leprous patients following their admission to the National Leprosarium

Type	Kolmer test			Kahn test			Combined Kolmer and Kahn tests		
	Number examined	Positive		Number examined	Positive		Number examined	Positive in one or both tests	
		No.	Percent		No.	Percent		No.	Percent
Tuberculoid.....	27	2	7.4	27	2	7.4	28	3	10.7
Neural.....	141	18	12.8	146	20	13.7	148	26	17.6
Lepromatous.....	200	110	55.0	196	109	55.6	203	123	60.6
Mixed.....	308	147	47.7	310	150	48.4	317	177	55.8
Total.....	676	277	41.0	679	281	41.4	696	329	47.3

From the above table it is noted that 47.3 percent of all types of leprous patients admitted to the National Leprosarium had positive Kolmer and Kahn tests (one or both). There were 41 percent of 676 with positive Kolmer and 41.4 percent of 679 with positive Kahn tests. Close agreement between these two serologic procedures in leprosy is thus demonstrated. It is interesting to note that while only 10.7 percent of tuberculoid and 17.6 percent of patients with neural leprosy gave positive tests, 55.8 percent of those with mixed and 60.6 percent of the lepromatous cases gave such reactions. This conforms with the experience of other writers.

In the whole group of patients there were 239 in whom the Kolmer and Kahn tests were repeated from once to several times during the period of hospitalization. In 147 of these patients the results of the tests remained practically unchanged upon each reexamination. As a rule, in these patients no marked changes occurred in the activity of the disease during the period of observation. In the remaining 92 patients, on whom repeated tests were performed, definite changes

were observed in the serologic reactions toward either the positive or the negative side. In 68 of them the tendency was for the tests to become more positive and in 24 for them to become less positive or negative.

Among the 68 patients exhibiting a tendency toward greater positivity, there were 39 in whom both Kolmer and Kahn tests changed from negative on admission to positive on final retesting. In the other 29 patients only one test became positive when previously negative; thus with both tests originally negative, one was subsequently positive, or, with one positive and one negative test to start with, both were positive on the last examination.

With but few exceptions, the phenomenon of increased positivity in the serologic reactions in leprosy was accompanied by a definite increase in the clinical manifestations of the disease, and decreased positive or negative reactions were observed with improvement or arrest of the disease. In 68 cases the parallelism between increasingly positive serologic reactions and progression of the disease was clearly shown.

Among 24 additional patients in whom the Kolmer and Kahn tests became less positive, there was a complete reversal from positive to negative in 12 and a partial change towards the negative side in the other 12. It was generally noted that the decrease in intensity of the serologic reaction accompanied a corresponding recession in leprosy. It was usually found that when clinical improvement continued to the point of arrest of the disease, the Kolmer and Kahn test both reverted to negative.

From these findings it is evident that changes in serologic reactions during the course of leprosy are closely correlated with changes in the activity and clinical manifestation of the disease. The writers believe that this suggests the presence of an antibody in the serum of leprosy patients capable of reacting positively with Kolmer and Kahn antigens in the absence of syphilis. This antibody, fluctuating with the extent and activity of leprosy, accounts for the changes in the serologic reactions in certain patients.

The majority of patients in whom the Kolmer and Kahn tests changed from negative to positive were under continuous hospitalization at the leprosarium during the whole period. No evidence of primary or secondary syphilis was observed to develop in any of this group of patients to account for the change in serologic reactions.

Of the 68 patients showing this change in serologic reactions from negative to positive, there was definite advance in the disease, with but few exceptions. Thirty-six of these patients have since died of the disease or its complications, and most of those still living are in the terminal stages of the lepromatous or mixed type of leprosy.

A large number of patients (82 percent) entering the leprosarium with maculo-anesthetic or neural leprosy show negative Kolmer and Kahn tests on admission. In some of these patients the disease progresses, and the superimposition of lepromatous lesions produces a mixed type of disease. Repeated serologic tests in a number of these patients show

strongly positive reactions with both Kolmer and Kahn antigens by the time the disease has advanced to the mixed stage. Twelve such cases were recorded.

The large majority of patients in whom the tests reverted from positive on admission to negative later in the course of the disease were also under constant observation and care at the leprosarium during the intervening period. None of these patients received antisyphilitic therapy during that time. It is interesting to note that of the 12 patients in whom a complete reversal of the Kolmer and Kahn tests from positive to negative occurred, the disease had become arrested in 10 shortly before or after the serologic reaction became entirely negative.

During the period under consideration, 134 leprosy patients with positive serologic reactions, the majority of whom had 4 plus Kolmer and Kahn reactions, died and were examined post mortem. In over 90 percent of these cases no evidence of syphilis could be found at the postmortem examination. This is another link in the chain of evidence showing that leprosy causes biologically false positive serologic tests for syphilis.

During the year 1932 a number of patients of the National Leprosarium with positive Kolmer and Kahn tests were given antisyphilitic medication in the form of neoarsphenamine and bismuth as a therapeutic test. In none of 16 such patients, in whom Kahn and Kolmer tests were subsequently repeated, did reversal of serologic reaction from positive to negative occur. In 2 patients there was a slight shift, from 4 plus to 2 plus in the Kolmer in one and from 4 plus to 3 plus in the Kolmer in the other. This is further evidence that in leprosy a positive serologic reaction generally stems from the disease itself rather than from complicating syphilis.

#### CAUSATIVE FACTOR OF POSITIVE SEROLOGIC REACTIONS IN LEPROSY

In a search for the factor responsible for the positive Wassermann and Kahn tests in leprosy, it seemed feasible to study the serum globulins. It is well known that leprosy, even more than syphilis, pro-



duces a hyperglobulinemia. It was thought that a study of the percent of serum globulin and of the albumin-globulin ratio in the patients at the National Leprosarium might throw some light on the subject. Should there be a correlation between the hyperglobulinemia or the reversal of the albumin-globulin ratio and the degree of positivity of the Kolmer and Kahn reactions, it would suggest the

presence of the causative antibody in the globulin factor of the blood serum.

That this study revealed a suggestive relationship between the globulin content of the serum and the blood serologic reaction in leprosy is shown in tables 2 and 3. The correlation is not consistent in all cases, and before conclusions can be drawn further experimental study must be undertaken.

TABLE 2.—*Relation of serum proteins and albumin-globulin ratio to serologic tests in leprosy*

Kolmer and Kahn tests	Number of cases	Range of total proteins (percent)			Range of serum albumin (percent)			Range of serum globulin (percent)			Albumin-globulin ratio		
		High	Low	Average	High	Low	Average	High	Low	Average	High	Low	Average
Both positive--	66	10.1	4.6	6.9	4.6	1.5	3.0	7.6	2.0	3.9	1.9	0.3	0.9
Both negative--	60	8.7	4.7	6.9	4.9	2.1	3.7	5.7	1.5	3.1	3.1	0.4	1.2

TABLE 3.—*Range of serum proteins in relation to serologic reactions of leprosy*

Kolmer and Kahn tests	Number of cases	Total protein (normal range 6 to 8 percent)						Serum albumin (normal range 3.9 to 5.72 percent)						Serum globulin (normal range 1.7 to 3.2 percent)						Albumin-globulin ratio (normal range 1.5 to 2.5)					
		Above normal range		Within normal range		Below normal range		Above normal range		Within normal range		Below normal range		Above normal range		Within normal range		Below normal range		Normal or above		Below 1.5		Reversed A/G ratio below 1	
		Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Both positive-----	66	11	16.7	43	65.2	12	18.2	0	0	3	4.5	63	95.5	43	65.2	23	34.8	0	0	5	7.6	61	92.4	40	60.5
Both negative-----	60	5	8	50	83	5	8	0	0	24	40	36	60	31	52	26	43	3	5	15	25	45	75	16	27

The normal values of serum albumin and serum globulin range from 5.72 to 3.9 percent and 3.22 to 1.7 percent, respectively (6). The total serum proteins range normally from 6 to 8 percent. The normal albumin-globulin ratio varies from 1.5:1 to 2.5:1.

Tables 2 and 3 demonstrate the increased globulinemia in leprosy. This increase in globulin and the reversal of the albumin-globulin ratio are more marked when the blood serologic reaction is positive than when it is negative. While the total proteins have a tendency to be slightly decreased, they are for the most part within normal range. Serum albu-

min is considerably diminished, and serum globulin is definitely increased. This increase in serum globulin is present in 65 percent of Kolmer and Kahn positive cases, in contrast to 52 percent of negative reactors.

It has been found that the progress of several infections is associated with changes in serum protein which produce an increase in total globulins and a lowering of the albumin-globulin ratio. Some of these infectious diseases in which there is definite increase in the globulin content of the blood serum are kala-azar, schistosomiasis, malaria, pneumonia, active pulmonary tuberculosis, yaws, syphilis, and



leprosy. All of these, to a greater or less extent, are liable to give positive complement fixation and flocculation tests for syphilis.

It is well known that it is the globulin factor of the serum proteins which contains the antitoxins and immune bodies. The flocculation tests for syphilis seem dependent upon an excess of globulin in the patient's serum. Antibodies responsible for the complement fixation reactions are also found to be contained in the globulin portion of the serum, whether in the pseudoglobulin or euglobulin not having been definitely determined.

Globulin is a complex factor containing several different components, at present called alpha, beta and gamma globulin. In older textbooks serum globulins were divided into pseudoglobulin I, pseudoglobulin II, and euglobulin. A new test for malaria is based upon an increase in the euglobulin content of the blood serum (7). This test would probably also be positive in leprosy.

Which of the globulin components, if any, contains the antibody which produces a positive serologic reaction in leprosy, syphilis and other diseases is still undetermined. It is at present well substantiated that the average globulin content in leprosy blood is very high and much higher than the average globulin content of the blood serum in syphilis. It has been shown that it is the euglobulin component (8) which is increased in leprosy.

#### CONCLUSIONS

Kolmer, Kahn and other tests for syphilis are frequently positive in leprosy.

Positive tests occur more frequently in lepromatous and mixed cases than in neural and tuberculoid leprosy.

Positive blood serologic reaction occurs in leprosy in the absence of syphilis and yaws.

Changes in the extent and activity of the disease are often reflected in corresponding changes in the patient's serologic reactions.

This seems to indicate that leprosy serum contains an antibody or reagent capable of reacting positively with Kolmer and Kahn antigens, and that this antibody fluctuates in accordance with advances and recessions in the disease.

There is suggestive evidence to the effect that this antibody is contained in the euglobulin component of leprosy blood serum.

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# An Evaluation of the Blood-Dye Diluent for the Transportation of Material from Gonococcic Infections

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One of the chief problems in the diagnosis of gonorrhea is the difficulty encountered in the transportation of specimens to the laboratory for cultural study. Vonderlehr (1) recently expressed the views of those interested in the control of gonococcic infection when he stated that venereologists "await with eagerness the description of a cultural method for the gonococcus which has a simple technic for the collection of the specimen by the physician in general practice and which may be transmitted under ordinary conditions to the laboratory for incubation. A cultural method of this kind would not only greatly improve the diagnosis of gonococcic infection, but would aid materially in the more difficult problem of the determination of the period of communicability in the individual case."

Many attempts have been made to arrive at a solution to this problem by improving cultural methods (2, 3, 4, 5), by modifying secretions so that the gonococcus would remain viable while being transported to the laboratory (6, 7, 8), and through the development of selective diluents (9, 10) and media (11, 12, 13, 14) which inhibit the growth of contaminating organisms without affecting the vitality of the gonococcus. Greene and Breazeale (15) suggested the use of swabs impregnated with ascitic fluid similar to the Brahdy swabs used in the laboratory diagnosis of diphtheria. Though these swabs are of some value in maintaining the viability of the gonococcus, they fail to inhibit the growth of concomitant organisms at the temperatures to which they are submitted while in transit. Sanderson and Allison (16) later found swabs im-

pregnated with beef blood to be unsatisfactory due to overgrowth from contaminating bacteria frequently present in the secretions.

Wortman and his associates (7) reported a method for the preservation of the gonococcus in frozen urine and broth. The method consists essentially of rapidly freezing the specimens in a mixture of dry ice and 95 percent ethyl alcohol, preserved in a frozen state in a container packed with dry ice, and shipped to the laboratory for examination. They suggested that the freezing method might be of value particularly in the diagnosis of gonorrhea in female patients where the result of microscopic examination of spreads is frequently inconclusive. These observations were confirmed by Sanderson and Allison (16). However, they indicate that the method described would be useful only to practitioners who are within 24 hours' mailing distance of a laboratory. Instead of placing the swabs in broth which was subsequently frozen, these authors impregnated swabs with 15 percent glycerine made up in a buffer mixture at approximately pH 7.4. The necessity of keeping specimens frozen during transit presents a disadvantage since dry ice is not available in many places. This has been overcome to some extent by Heathman and Higginbotham (17) and Price (18) who shipped cultures in thermos jars.

Several attempts have been made in this laboratory (19) during the past 2 years to arrive at a suitable procedure for making the cultural method available to the practicing physician. Attempts were made to develop a selective diluent which would permit the growth of the gonococcus and inhibit the growth of certain contaminating organisms, using dyes of the triphenylmethane series. Of the dyes tested (gentian violet, iodine green, brilliant green, methyl violet, basic fuchsin), none fulfilled the necessary requirements. Preliminary studies have

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indicated that gentian violet suppresses the great majority of gram-positive bacteria, but the gonococcus was also susceptible to its toxic action. Similar results with the triphenylmethane dyes have been reported by Cook and Stafford (20), Erickson and Albert (21), Torrey and Buckell (11), and others. Torrey and Buckell found that the gonococcus exhibits only a slightly lower degree of susceptibility to the bacteriostatic action of gentian violet than do the gram-positive cocci, and classified the gonococcus as a "gentian violet positive organism."

The ability of Nile blue A to inhibit the growth of contaminating organisms in gonococcus cultures has been reported by Gardner (12) and confirmed by Peizer and Steffen (22). The latter investigators incorporated the Nile blue A dye in proteose-peptone plasma hemoglobin agar and found that it reduced the number of contaminants and proved to be of value in the isolation of the gonococcus, especially in cultures from females.<sup>2</sup> Recently Cox, McDermott and Mueller (9) reported a method for the delayed planting of gonococcus cultures. These investigators tested several dyes and found that gentian violet in a dilution of 1:30,000 in defibrinated horse blood inhibited the growth of many organisms, but permitted the gonococcus to remain viable for long periods of time.

The present study was planned with the view of evaluating the blood-dye diluent described by Cox and his associates (9). The specimens used were obtained from both male and female patients attending the clinics of the Venereal Disease Control Service of the St. Louis Health Division,<sup>3</sup> and some specimens were obtained from men in the military service.<sup>4</sup>

<sup>2</sup> These investigators have since discontinued the use of Nile blue A and have substituted cysteine monohydrochloride in a final concentration of 0.03 to 0.05 percent.

<sup>3</sup> The authors are indebted to the staff of the Venereal Disease Control Service for supplying the specimens.

<sup>4</sup> The authors are grateful to Maj. Leroy J. Stephens for kindly supplying specimens from cases of acute gonococcal infection among men in the Armed Forces.

The exudates were collected at the time of the patient's routine visit to the clinic. Material collected from the urethra in the male and from the cervix and the urethra in the female was used to make spread preparations for microscopic examinations and for inoculation of the blood-dye diluent. When specimens were collected from two areas, as in the female (cervix and urethra), a single tube of diluent was inoculated by a swab from each area. Separate sterile swabs were used for making the spreads and cultures. The secretions were collected in the usual manner. In obtaining specimens from the cervix, the cervical canal was cleansed with sterile cotton, and material from the deep cervical glands was obtained by compressing the portio between the plates of the speculum to force the contents of the deep racemose glands into the cervical canal. In obtaining specimens from the male the glans penis was not cleansed.

The cultural technic used in this study has been described in detail by one of us (S. E. S. (5)). During part of this study the culture medium used (proteose peptone #3-hemoglobin agar) was modified. An enriching factor (yeast autolysate) together with a bactericidal and bacteriostatic dye (crystal violet) was added.<sup>5</sup> Later the medium described by Peizer and Steffen (22) and containing cysteine monohydrochloride instead of Nile blue A, as suggested by Peizer (24), was used.

In the text "routine cultures" refer to those planted immediately, while "delayed cultures" refer to those planted after remaining at room temperature (varying between 68° F. and 85° F.) for 24, 48, 72 and 96 hours, respectively.

When the blood-dye broth of Cox and associates was first tested it was thought that the discouraging results were due to the use of a supply of gentian violet low in bactericidal and bacteriostatic properties. Dr. Oscar F. Cox was kind enough to send us a supply of the dye<sup>6</sup> which

<sup>5</sup> The use of the yeast autolysate and crystal violet was recommended by Christensen (23).

<sup>6</sup> This dye (lot No. C1681), which was furnished by the National Aniline & Chemical Co. and contained an 84 percent dye content, proved to be the same lot which was in use in our experiments.



he was using in his experiments. Specimens from 192 patients were examined, using the original diluent<sup>7</sup> recommended by these investigators (9). Later, specimens from 94 additional patients were examined, using a slightly modified diluent<sup>8</sup> described by Cox and McDermott (10). Since the results with these two diluents were essentially the same, the data are combined to facilitate presentation.

Throughout all experiments the method of recording observations was essentially the same. Comparisons of the results of the routine and delayed cultures were made by estimating the total number of gonococcus colonies, as well as colonies of other bacteria.

### RESULTS

Table 1 shows the results of laboratory examinations of material collected from 125 male patients with gonococcal infection. Routine microscopic examination of specimens from these patients showed *intracellular* gram-negative diplococci resembling gonococci. All routine cultures in this group of patients were positive. The number of positive delayed cultures, together with the estimated number of gonococcus colonies, is indicated for the various periods of time the specimen remained in the blood-dye diluent between collection of the material and planting. Of the 125 specimens known to contain gonococci, 74.40 percent were positive when planting was delayed for 24 hours, 39.27 percent were positive after 48 hours, 15.20 percent were positive after 72 hours, and only 2.40 percent were positive after 96 hours. The delayed cultures were invariably more contaminated than the routine cultures.

<sup>7</sup> Sterile defibrinated horse blood is added in equal amounts to an aqueous solution of gentian violet (sterilized in the autoclave), so diluted to make a final dilution of 1:30,000 of the dye. The blood-dye diluent is tubed aseptically.

<sup>8</sup> Sterile defibrinated horse blood is diluted with an equal amount of sterile distilled water and added in equal amounts to 1 percent aqueous solution of gentian violet to make a final dilution of 1:30,000. Para-aminobenzoic acid (5 mg. percent) is added before the blood-dye diluent is dispensed in sterile tubes.

TABLE 1.—Specimens from one hundred and twenty-five (125) male patients with gonococcal infection

[Routine microscopic examination showed intracellular, gram-negative diplococci resembling gonococci.]<sup>\*</sup>

"Routine" culture #		Total elapsed hours between collection of specimen and planting. †			
Estimated number of gonococcus colonies	Number of cultures	24	48	72	96
1 to 10.....	\$16	\$7	3	0	0
11 to 25.....	46	32	19	4	1
26 to 50.....	41	36	12	2	0
51 and over.....	22	18	15	13	2
Total.....	125	93	49	19	3
Percent positive.....	100	74.40	39.27	15.20	2.40

\*Specimens which showed intracellular gram-negative diplococci morphologically indistinguishable from the gonococcus and which were negative by the "routine" culture method were omitted from this tabulation.

†Specimens planted immediately after collection.  
‡Specimens maintained at room temperature in the blood-dye diluent.

§Figures indicate number of positive cultures.

When only a few gonococci (1 to 10 colonies per plate) were present in the original specimen, delayed cultures were negative after 72 and 96 hours. In many instances, where a large number of organisms were present in the exudate, routine cultures which contained numerous gonococci (more than 51 colonies per routine culture) yielded positive delayed cultures after 96 hours.

The results of laboratory examinations of cervical and urethral specimens obtained from 98 female patients with gonococcal infection are not as encouraging as those presented in table 1. The routine microscopic examination of specimens from these patients showed *intracellular* gram-negative diplococci morphologically indistinguishable from the gonococcus. The results summarized in table 2 show that 51.02 percent of the cultures were positive when planting was delayed for 24 hours, while only 16.31 percent were positive after 48 hours. Only 1 of 4 specimens which contained numerous gonococci in the original exudate (more than 51 colonies per routine culture) was positive when planting was delayed for 72 hours. No positive cultures were obtained

TABLE 2.—*Specimens from ninety-eight (98) female patients with gonococcic infection*

[Routine microscopic examination showed intracellular gram-negative diplococci resembling gonococci] \*

"Routine" culture #		Total elapsed hours between collection of specimen and planting.†			
Estimated number of gonococcus colonies	Number of cultures	24	48	72	96
1 to 10.....	§ 44	§ 18	3	0	0
11 to 25.....	38	21	9	0	0
26 to 50.....	12	8	2	0	0
51 and over.....	4	3	2	1	0
Total.....	98	50	16	1	0
Percent positive.....	100	51.02	16.31	1.02	0

\* Specimens which showed intracellular gram-negative diplococci morphologically indistinguishable from the gonococcus and which were negative by the "routine" culture method were omitted from this tabulation.

† Specimens planted immediately after collection.

‡ Specimens maintained at room temperature in the blood-dye diluent.

§ Figures indicate number of positive cultures.

when planting was delayed for 96 hours. In this series of specimens the delayed cultures were also more contaminated than the routine cultures, indicating that the blood-dye diluent failed to inhibit the growth of at least some of the concomitant organisms present in the exudates.

The secretions from 63 additional female patients with gonococcic infection were tested as indicated above and the results are presented in table 3. Microscopic examination of specimens from these patients showed extracellular organisms indistinguishable from the gonococcus and all routine cultures were positive. In this series of specimens only 39.68 percent of the cultures were positive when planting was delayed for 24 hours and 4.76 percent were positive after 48 hours. No positive cultures were obtained when planting was delayed for 72 and 96 hours.

A summary of the results of all the specimens from both the male and female patients is presented in table 4. Of the 286 specimens examined, 50.87 percent were positive when planting was delayed 24 hours; 23.77 percent were positive after 48 hours; 7.0 percent were positive after

72 hours, and 1.05 percent were positive after 96 hours. The loss of 49.13 percent of positives when planting is delayed for only 24 hours is obviously too great to warrant routine use of this diluent. Generally, better results were obtained with specimens obtained from white patients than those obtained from Negro patients. The delayed cultures of specimens from the Negro patients were more frequently contaminated than those obtained from the white patients.

During the time this manuscript was in preparation, Peizer and Steffen (25) reported an improved method of transportation of material from gonococcic infection. They found that by transporting material on plasma-hemoglobin agar (22) the loss of positives was reduced from 52 to 11 percent when specimens were planted in broth or directly on agar, respectively, and maintained at room temperature for 20 to 24 hours. When cysteine monohydrochloride in a final concentration of 0.03 percent was added to the plasma-hemoglobin medium, only about 2 percent of the positives were lost when the cultures were kept at room temperature for 24 hours prior to incubation at 37° C in an atmosphere of CO<sub>2</sub>.

TABLE 3.—*Specimens from sixty-three (63) female patients with gonococcic infection*

[Routine microscopic examination showed extracellular gram-negative diplococci resembling gonococci] \*

"Routine" culture #		Total elapsed hours between collection of specimen and planting.†			
Estimated number of gonococcus colonies	Number of cultures	24	48	72	96
1 to 10.....	§ 43	§ 14	2	0	0
11 to 25.....	9	4	0	0	0
26 to 50.....	9	6	0	0	0
51 and over.....	2	1	1	0	0
Total.....	63	25	3	0	0
Percent positive.....	100	39.68	4.76	0	0

\*Specimens which showed extracellular gram-negative diplococci morphologically indistinguishable from the gonococcus and which were negative by the "routine" culture method were omitted from this tabulation.

†Specimens planted immediately after collection.

‡Specimens maintained at room temperature in the blood-dye diluent.

§ Figures indicate number of positive cultures.



TABLE 4.—Summary of results of specimens from two hundred and eighty-six (286) male and female patients with gonococcal infection

Sex	Race	"Routine" spreads*	"Routine" cultures #	Total elapsed hours between collection of specimen and planting. †			
				24	48	72	96
Male.....	White.....	Intracellular.....	§ 36	§ 40	18	12	2
	Negro.....	Intracellular.....	89	53	31	7	1
Female.....	White.....	Intracellular.....	46	18	6	1	0
	Negro.....	Intracellular.....	52	32	10	0	0
Female.....	White.....	Extracellular.....	29	11	3	0	0
	Negro.....	Extracellular.....	34	14	0	0	0
Total.....			286	168	68	20	3
Percent positive.....			100	50.87	23.77	7.0	1.05

\* "Intracellular" indicates that intracellular gram-negative diplococci indistinguishable from the gonococcus were present.

"Extracellular" indicates that extracellular gram-negative diplococci indistinguishable from the gonococcus were present.

# Specimens planted immediately after collection.

† Specimens maintained at room temperature in the blood-dye diluent.

§ Figures indicate number of positive cultures.

Experiments are now in progress to determine the practicability of this improved transportation medium.

#### CONCLUSION

The use of the blood-dye diluent is not recommended for general use because of the high incidence of negative cultures when planting is delayed for 24 hours or more.

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## DIAGNOSIS

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**The accuracy and interpretation of modern blood tests for syphilis.** Earle K. Borman. Connecticut M. J., Hartford, 8: 82-93, Feb. 1944.

The author has discussed the accuracy and interpretation of modern blood tests for syphilis primarily for the general practitioner. He has compiled data from carefully controlled studies of the sensitivity and the specificity of five tests: the Mazzini flocculation, the Connecticut complement fixation, the Kolmer complement fixation, the Hinton, and the standard Kahn.

The Mazzini flocculation test has proved to be much more efficient in detecting syphilis of long standing than the other tests discussed. The Connecticut complement fixation test was found slightly less sensitive than the Mazzini. The Connecticut Bureau of Laboratories has selected these two tests as routine procedures on the theory that a public health laboratory should direct attention to syphilis in the latent stage as well as detect syphilis which is clinically active. When two tests for syphilis are reported as one positive and one negative, it is not a doubtful re-

sult. This type of finding is usually due to difference in sensitivity, and the probability is that the positive test is the best guide in diagnosis. Exclusion of laboratory error requires the submission of at least one repeat specimen whenever positive or doubtful laboratory findings are encountered in the absence of clinical findings. It is the physician who makes the diagnosis, but often solely on the basis of laboratory findings. Occasionally the blood test will fluctuate from week to week; this is more often encountered in persons who have been under treatment at some time than in untreated cases, though it can occur in the later.

Every laboratory making tests for syphilis should maintain a consistently high level of performance by adhering to a rigid technic and by resorting to frequent inter-laboratory checks. The physician must not expect a ready-made diagnosis from specialized laboratory service; it is simply an aid, providing a greater range of information than the routine tests.

Dr. Allen K. Poole discussed the paper, and he emphasized that, in spite of laboratory help, the burden of proof or establishing a diagnosis of syphilis rests in the hands of the clinician. The physician's reliance on the serologic test should be tempered by the knowledge that the tests are not foolproof.

**The meatal chancre.** Charles Lee McCarthy. U. S. Nav. M. Bull., Washington, 42: 431-432, Feb. 1944.

The clinical appearance of a syphilitic chancre in the meatus is misleading, since it does not correspond to the chancre in other parts of the body. As a rule the disease is diagnosed as a mild form of gonorrhea or a recurrence of an old gonorrhea, because of the absence of pain and the presence of serosanguineous urethral discharge. This finding should always make the physician suspicious that he is dealing with a mixed infection of syphilis and gonorrhea.

Induration of the lesion is a sign of utmost diagnostic importance. The induration can be readily felt by holding the penis between the thumb and forefinger and palpating it in an auteroposterior

direction. If the possibility of the lesion being syphilitic is recognized, the diagnosis is no longer a clinical problem; the clinical suspicion should be verified by repeated darkfield examination. The meatal chancre in its earliest stages may have the exact appearance of an abortive type of herpes genitalis located partially in the meatal opening and partially on the surrounding surface. All such lesions should be subjected to immediate and repeated darkfield examinations.

**The vesicular reaction in the diagnosis of lymphogranuloma inguinale.** (La reacción vesicular: metodo para el diagnostico de la infección por virus poradenico.) C. Ottolina. Rev. Policlín. Caracas, 12: 13-20, Jan.-Feb., 1943. Abs. in Bull. Hyg., London, 19: 32, Jan. 1944.

The author has devised a method of testing for lymphogranuloma inguinale which he considers more accurate than the Frei test. This test may be made at the same time as the Frei test. Ten cc. of cerebrospinal fluid is obtained from a positive case. This is concentrated down to 1.5 cc.; 0.3 cc. of this concentration is injected intradermally and, in a positive case, a vesicle appears in 24 hours. The tint of the skin over it is dark grayish, darker than the adjacent skin. In 48 hours the tension in the vesicle lessens and umbilication may be seen; in 3 days it is flaccid and begins to dry up. The fluid is yellow and viscid, contains mononuclear and polymorphonuclear cells, but no bacteria.

In 5 Frei-positive cases with anorectal syndrome all were positive to the author's test; in 5 Frei-positive cases without genitoretal symptoms all gave positive results to this test, and 2 Frei-negative cases with rectal stricture gave negative results to this test.

Repetition of the test on the same individual seems to desensitize the patient.

**Syphilitic aortitis and aneurysm.** Aaron Arkin. M. Clin. North America, Philadelphia, 28: 70-85, Jan. 1944.

Syphilitic heart disease is preventable. A diagnosis in the primary seronegative

stage of syphilis by darkfield examination, followed by 2 years of proper treatment, would prevent at least 90 percent of cases of cardiovascular syphilis. Syphilis is responsible for about 20 percent of the cases of chronic cardiac disease in adults. The average length of time from infection to the onset of symptoms is about 15 years; in syphilitic aortic regurgitation the average latent period is 20 years, and in aneurysm 22 years. Many cases are recognized only after death.

About 80 percent of the cases of syphilitic heart disease are in males. This condition is seen four times as frequently in the Negro as in the white. While aneurysm is rare in white women, it is frequently found in Negro women.

The author stresses the importance of a periodic careful physical examination and roentgenographic study of every patient with evidence of syphilis. The diagnosis of uncomplicated aortitis is possible in a considerable percentage of all cases. The most valuable aids in diagnosis are: (1) Careful fluoroscopic examination, (2) tambour aortic second sound, (3) increased manubrial dullness especially in the second and third intercostal spaces, (4) visible pulsation in the second or third intercostal space or suprasternal, (5) difference in the radial or carotid pulse, and (6) angina pectoris in a young adult in the absence of other cause.

**Chancroid, lymphogranuloma venereum, and granuloma inguinale.** Bull. Genito-infect. Dis., Boston, 7: 1-4, Jan. 1944.

The majority of the States require that chancroid be reported and some States provide also for the reporting of lymphogranuloma venereum and granuloma inguinale. Recent legislation in Massachusetts has defined and made reportable these three diseases in addition to syphilis and gonorrhea.

Although chancroid, lymphogranuloma venereum and granuloma inguinale are more prevalent in the tropics and semitropics, cases have been reported in United States and Canada. In 1923, Shattuck reported 3 cases of granuloma inguinale in Boston.



Under the present conditions of mobilization of troops the epidemiologic importance of chancroid, lymphogranuloma venereum and granuloma inguinale is apparent, and more provision for the study, diagnosis and treatment of these diseases should be made available. One large Army camp in Massachusetts reported 28 cases of chancroid, 27 cases of lymphogranuloma venereum and 4 cases of granuloma inguinale during 1943. With the return of men who have been stationed in tropical and semitropical regions, it is possible that some parts of the country may experience an increase in these diseases.

The treatment of chancroid and lymphogranuloma venereum with the sulfonamides is generally satisfactory, and most cases of granuloma inguinale respond to various antimony preparations given intravenously with or without the use of roentgen therapy.

Chancroid, lymphogranuloma venereum and granuloma inguinale are discussed in respect to their symptoms, prevalence, diagnosis and treatment.

**The technique of cisternal puncture in the modern treatment of syphilis.** Leo Spiegel. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, 28: 96-102, Jan. 1944.

The author presents a summary of his experience with cisternal puncture based on about 10,000 punctures during the past 15 years. He has used this method in obtaining spinal fluid since 1927 at both the New York University Clinic and the Lenox Hill Hospital. The technic, which he describes in detail, is a combination of the indirect method of Eskuchen and the direct method of Ayer.

Cisternal puncture by a qualified physician is a safe and simple procedure, ideally adapted to routine clinic and office use. Used chiefly for diagnostic purposes in the management of syphilis and neurosyphilis, it possesses definite advantages over lumbar puncture.

From his experience, the author states that it is impossible to determine beforehand, with any degree of accuracy, whether one is able to touch the posterior edge of the foramen magnum of the occip-

ital bone before puncturing the dura in entering the cisterna magna. All external landmarks should be disregarded except the occipital protuberance, the spinous process of the axis, or second vertebra and the deepest depression at the back of the neck.

Some contraindications to the use of the cisternal puncture are infections at the back of the neck and arteriosclerosis.

**Syphilitic juxta-articular nodules.** Frederick Kalz and B. L. Newton. *Arch. Dermat. & Syph.*, Chicago, 48: 626-634, Dec. 1943.

The few cases reported in the literature seem to indicate that syphilitic juxta-articular nodules are comparatively rare in North America, but in many instances they have been diagnosed as fibromas. The presence of syphilis, diagnosed clinically and serologically, a carefully taken history, a histologic examination, and observation of the subsequent course are all essential in order to diagnose this disease correctly.

The authors' case was that of a 71-year-old American Negro, admitted to the Royal Victoria Hospital because of pains in the right ankle. He had had gonorrhea several times, and a painful ulcer on the penis in 1907, which he treated with cupric sulfate. He was not aware of his syphilitic condition. He stated that a small hard growth on the right knee had appeared 1 year after the penile ulcer, followed by a similar one on the left knee, another on the left elbow 5 years later, and one on the right elbow 21 years after the appearance of the first growth. These tumors grew slowly without causing any discomfort until shortly before he entered the hospital. Upon examination, a diagnosis of late syphilis with juxta-articular nodes, aortitis and aneurysm of the innominate artery, and asymptomatic inactive neurosyphilis was made.

The nodules were removed surgically and antisyphilitic treatment with bismuth subsalicylate and potassium iodide was started. Small nodules on the right ankle had decreased in size 3 months after treatment was begun. Histologic examination of the nodes demonstrated exten-



sive degenerative changes in some, while the more recent ones resembled simple fibroma. No *Treponema pallidum* could be found.

One of the authors (F. K.) saw similar nodules in another patient. She had a hard tumor, the size of a cherry, close to the right elbow and a circinate nodular syphilid on the extensor surface of the right arm. Histologic examination of the tissue from this syphilid revealed foci of tuberculoid structure almost indistinguishable from lupus vulgaris. This syphilid disappeared after 3 weeks' therapy, and the node gradually decreased to about half its size during 2 years of intensive antisypilitic treatment.

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## TREATMENT

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**The clinical use of penicillin: Observations in one hundred cases.** Martin Henry Dawson and Gladys L. Hobby. J. A. M. A., Chicago, 124: 611-622, Mar. 4, 1944.

Studies on penicillin have been carried on at the Presbyterian Hospital since the fall of 1940. Experimental work had clearly demonstrated that penicillin was primarily effective against gram-positive organisms, both cocci and rods, and against gram-negative cocci. Since it was further recognized that effective sulfonamide therapy was available for many infections caused by these organisms, treatment was largely restricted to those infections in which gram-positive organisms and gram-negative cocci played a dominant role and in which sulfonamide therapy was known to be ineffective. Treatment was administered by the intramuscular, the intravenous and the intrathecal routes, the first being the route of choice. From the beginning of clinical trials the problems of correct dosage and frequency of administration were complex. Certain strains in gonococcus and meningococcus were found to be the most sensitive. In blood stream infections and acute infections of the genitourinary tract due to gonococci, 10,000-15,000 units every 4

hours intramuscularly were given. Two days' therapy was usually adequate. In general the initial dose recommended is the same as subsequent doses.

Since the intramuscular route appears to be the route of choice in most types of infections, and since frequent administration is essential, it is desirable that the drug be given in as small a volume as possible. The sodium salt is readily soluble in isotonic solution of sodium chloride and can be conveniently administered in amounts of 5,000 units per cc. Penicillin resistant strains of gonococci have not been encountered.

The number of cases of gonococcal infection treated is limited, but the results have been satisfactory. Eight cases are reported, 6 of urethritis and 2 of arthritis. The urethritis cases had been completely resistant to sulfonamide therapy. All responded to penicillin and were cured from a clinical and bacteriologic standpoint within 48 hours. The dose was 10,000 to 15,000 units every 3 to 4 hours for 2 days.

The results in the cases of gonococcal arthritis were equally satisfactory. The first was a case of arthritis of the wrist with early destruction of the joint. Sulfonamide therapy and other measures had proved completely ineffective. The response to penicillin was unequivocal within 48 hours and the final outcome was a normally functioning joint. The other case of arthritis was treated locally by the injection of 10,000 units daily for 3 days into the knee joint. The patient was discharged on the fifth day, all evidence of infection having subsided.

**The clinical use of penicillin, an antibacterial agent of biologic origin.** Wallace E. Herrell. J. A. M. A., Chicago, 124: 622-627, Mar. 4, 1944.

Practically all of the experimental and clinical reports which have appeared concerning the work on penicillin have had to do with the sodium salt of penicillin; the Oxford investigators in 1942 and in 1943 reported their observations on the calcium salt. In 50 of the 62 cases which have been treated at the Mayo Clinic, the sodium salt of penicillin was used, and

in 12 cases the calcium salt. Either of these salts may be applied locally or administered intravenously or intramuscularly. The calcium salt appears to be more stable. Experience in this group of cases seems to justify the conclusion that 40,000 units of penicillin per day is sufficient for the infections treated. The author has found the intravenous drip method to be the most satisfactory.

Among the 62 cases treated by penicillin at the Mayo Clinic were 16 cases of gonococcal infection, all sulfonamide resistant. In no instance was there failure. The duration of treatment was seldom more than 48 to 72 hours. It was never necessary to use more than 100,000 to 150,000 Oxford units of penicillin in these cases; complete cures were obtained by using as little as 65,000 units. The author says that probably the intramuscular administration is quite well adapted to these cases, but he has used the intravenous drip method, which permitted a longer period of treatment than was possible with the same amount of penicillin usually necessary for a 24-hour course of intramuscular injections. This seemed desirable since treatment was continued to the time when the first negative cultures were reported.

In the discussion of the papers in this symposium on penicillin (p. 637), Priest stated that he has given 500,000 units of penicillin in 100 cc. of water intravenously over 30 minutes and 40,000 units in 5 cc. of saline solution intrathecally without significant reaction. No toxic reaction followed administration of 1,000,000 units of the calcium salt intravenously over 7 days. Some observations indicate a bacterial effect of penicillin, but these are too limited to permit of definite conclusions.

**The clinical use of penicillin.** Arthur L. Bloomfield, Lowell A. Rantz and William M. M. Kirby. J. A. M. A., Chicago, 124: 627-633, Mar. 4, 1944.

The sodium salt of penicillin, as furnished to the authors, is a brown or yellow powder, put up in sealed glass ampules; it is extremely soluble in water and in saline or dextrose solution, 10,000

units or more being readily taken up in 1 cc. of fluid. The material is unstable in air and very hygroscopic; its potency is impaired by heat and in acid mediums. Since the exact constitution of penicillin has not as yet been worked out, the material cannot be standardized by chemical means but is assayed by its biologic effect. In Florey's original material there were 40 to 50 units per milligram, an Oxford unit being the amount of penicillin compared with an arbitrary standard which completely inhibits the growth of a test strain of *Staphylococcus aureus*. Material which runs 700 to 1,000 units per milligram has now been prepared.

The use of penicillin is not the simple matter which some believe. In their work at the Stanford University Hospital, the authors have found that a "penicillin team" was necessary to carry out the treatments effectively. They have used subcutaneous administration by the drip method extensively in their work, and they believe that this route is adequate in gonococcal infections. If the continuous intravenous drip cannot be given, intermittent intramuscular injections, perhaps combined with subcutaneous clisis, would be the best alternative.

The dosage has been largely arbitrary and as long as the material is so difficult to prepare, economy is of the utmost importance. The authors believe that it has been clearly established that most patients with acute and subacute gonorrhea can be sterilized (of gonococci) and clinically cured in a period of 1 or 2 days by doses of from 50,000 to 200,000 units given by a number of routes.

The authors say they have observed no toxic effects from penicillin.

Two cases are discussed which show that even after gonococcal infection has been present for months it can still be rapidly controlled. In many patients, a total quantity of 60,000 to 100,000 units given in divided doses intramuscularly or by continuous or intravenous drip was effective. The authors have confirmed the findings of Mahoney in 7 cases of early syphilis. In other cases condylomas have become free of treponemes in from



12 to 20 hours. Immediate results comparable to those obtained with full doses of arsphenamine can be achieved. Penicillin treatment for syphilis is being studied by especially appointed committees.

**Penicillin available for ophthalmia in newborn.** Medical News. J. A. M. A., Chicago, 124: 449, Feb. 12, 1944.

Twenty million units of penicillin have been made available to the Illinois State Department of Public Health by the National Research Council to use on a research basis for the treatment of newborn babies with ophthalmia. Although the silver nitrate law for the protection of babies' eyes has made ophthalmia rare in Illinois, about 30 newborn infants are hospitalized at State expense each year to prevent blindness from a type of ophthalmia that is contracted at birth from mothers infected with a venereal disease, the State health department reported. The 20 million units of penicillin which have been made available to the department are enough to treat 30 infants.

**Study of sulfathiazole in calomel ointment as a prophylaxis for gonorrhea: A preliminary report.** John B. Kaufman and Ammon B. Litterer. U. S. Nav. M. Bull., Washington, 42: 483-485, Feb. 1944.

In the Tijuana and San Diego area, during a 3-month survey, 2,016 men received intraurethrally sulfathiazole-calomel ointment as a prophylaxis for gonorrhea. This group had not used any prophylactic measures prior to reporting for treatment. One group comprised of 1,025 had visited Tijuana and 98 percent had contacted prostitutes; the remaining 991 had exposed themselves to infection in San Diego. One infection of gonorrhea was reported in each group, and each of these men was found not to have reported for treatment within the 2 hours after exposure.

The ointment was composed of sulfathiazole powder, 4 gm.; mercurous chloride, mild, 8 gm.; woolfat, anhydrous, 8 gm.; petrolatum, white, 8 gm. It is hoped that the addition of sulfathiazole to the

calomel ointment will not minimize the effectiveness of calomel as a prophylaxis against syphilis. Further studies with this ointment as a prophylaxis against chancroid, gonorrhea, and syphilis seem desirable.

**An intradermal test for the recognition of hypersensitivity to the sulfonamide drugs.** William B. Leftwich. Bull. Johns Hopkins Hosp., Baltimore, 74: 26-48, Jan. 1944.

A method of determining hypersensitivity to the sulfonamide drugs by positive skin tests is described by the author. The material used for this intradermal test was obtained from patients who had been receiving sulfonamide either by mouth or by the parenteral route for periods of from 1 to 15 days, with drug levels of 2 to 20 mg. percent. Into the flexor surface of the forearm 0.05 cc. of control serum and 0.05 cc. of each of the sulfonamide serums were injected intracutaneously. The size of the wheal and the diameter of the erythema were then measured every 5 minutes for 20 minutes. A difference between the size of the control wheal and the size of the test wheal of at least 4 mm. diameter was used as a criterion for positivity, rather than absolute size of test wheal. The test is simple to perform, may be easily and quickly interpreted, and has been found to be reliable. Of 30, definitely hypersensitive patients, positive skin tests were obtained in 28, or more than 90 percent.

This test is used as a precautionary measure before starting sulfonamide therapy in patients who have previously received one of the drugs and as a differential diagnosis of drug reactions. The fact that positive skin tests may be so consistently obtained in sensitive individuals is additional evidence that drug sensitivity is an allergic reaction. The sensitizing antigen may be a sulfonamide plasma protein combination which occurs in vivo in the circulating blood of patients during sulfonamide therapy, the sulfonamide perhaps acting as a hapten.

The author's investigations were based on 76 patients seen at Johns Hopkins Hospital from March to July 1943. A chart



showing the studies made of these 76 patients is given. The author believes that the failure of 3 patients in this series (2 of whom developed hepatitis and 1 hemolytic anemia as a result of sulfonamide therapy) to show positive skin reactions for the homologous sulfonamide, supports the belief that these latter reactions are due to direct toxic action of the sulfonamide rather than to hypersensitivity.

#### **A different concept of reactions following sulfathiazole readministration.**

R. C. Green, Morris L. Steckel and John M. Michener. *Mil. Surgeon*, Washington, 93: 399-405, Nov. 1943.

Ill effects following sulfathiazole readministration have been observed at the Station Hospital, Camp Haan, California. The records of 55 patients, to whom sulfathiazole was readministered with an interval of 9 or more days between the last day of the initial course and the last day of the repeat course, were reviewed. Six of the 55 patients (11 percent) experienced drug reactions during the readministration. Only half of these (5.5 percent) were of a febrile type. This incident of reaction is almost identical to 30 reactions (10 percent) occurring among the last 300 patients receiving a single course of sulfathiazole in this hospital. No reaction, including fever, was of greater severity than that commonly seen during initial sulfathiazole use. No unusual type of reaction, not ordinarily held to be a sign of sulfathiazole intoxication, was observed.

The authors found that readministration of sulfathiazole to the same individual is no more dangerous than is the initial use of the drug. Drug reactions such as fever have occurred as early as the second day of initial sulfathiazole administration, with no previous opportunity existent for possible sensitization. Drug reactions following administration of other sulfonamides were seen after an initial course of sulfathiazole had been given.

The authors say they are reticent about accepting the theory that "hypersensitivity" is responsible for causing the ma-

jority of prompt reactions occurring during sulfathiazole readministration. They discuss 3 cases which they feel substantiate this view.

**Primary syphilis treated by twenty-six week course of mapharsen and bismuth: Acute basilar meningitis with neuroretinitis developing during treatment.** Gerard A. De Oreo. *Arch. Dermat. & Syph.*, Chicago, 49: 109-110, Feb. 1944.

A 22-year-old white soldier with an ulcer on the ventral surface of the mid-shaft of the penis was seen by the author on July 20, 1942. The diagnosis of seropositive primary syphilis was confirmed by darkfield examination of lymph node material. Combined mapharsen and bismuth therapy was started, practically following the Army 26-week plan of treatment which was then coming into use. No reactions were seen after the first injection of the arsenical. At the end of the thirtieth week he had received 40 injections of mapharsen, a total of 2,400 mg., and 22 injections of bismuth, and seemed in good physical condition. Two days later a severe occipital headache developed and 10 days following completion of antisypilitic treatment the patient was hospitalized because of signs of severe, acute syphilitic basilar meningitis. The only indication of this complication early in the disease was the low titer of the serologic reactions and the speed with which it began to decrease, with complete reversal in 3 months. In the light of the relapse, the serologic reactions must be interpreted as a result of poor immunologic response rather than of prompt therapeutic effect.

Fever cabinet therapy combined with administration of neoarsphenamine resulted in clinical recovery and satisfactory improvement of the condition of the spinal fluid. In the 11 weeks during which artificial fever was induced, with an average temperature of 105° to 106° F., the patient received 13 injections of neoarsphenamine and 5 of bismuth subsalicylate. Examination showed no evidence of any neurologic abnormality and

his mental status was normal. He was transferred to the outpatient clinic to continue treatment.

**The toxicity of sulfadiazine: Observations on 1357 cases.** Norman Plummer and Charles Wheeler. *Am. J. M. Sc., Philadelphia*, 207: 175-184, Feb. 1944.

The toxic reactions that have appeared in patients treated with sulfadiazine or sodium sulfadiazine on all the services at The New York Hospital up to May 1, 1942, have been evaluated. There was a total of 1,357 patients treated with a daily dosage of 3, 4, or 6 gm. of sulfadiazine orally over a period of 2 days or more, or with at least 2.5 gm. of sodium sulfadiazine intravenously. In this entire group there was 1 fatality, a case of thrombocytopenia purpura which was attributed to sulfadiazine. Since this paper was written, an additional 1,496 patients have been treated in the hospital with sulfadiazine orally or sodium sulfadiazine intravenously without another fatality in the total of 2,853 cases treated.

Eight percent of 705 patients, who received 6 gm. of sulfadiazine daily for at least 2 days and not more than 14 days, showed evidences of toxicity. The renal reaction was the most frequent single toxic manifestation. With intravenous sodium sulfadiazine the incidence of renal reactions was almost doubled, and thereby the total incidence of reactions was raised.

The effect of previous use of sulfonamide therapy upon toxicity was observed in 87 patients, and in these there was a slightly increased incidence of reactions attributable to a slight drug rash, drug fever, and leukopenia.

The renal complications comprised more than half of the toxic reactions following sulfadiazine in the entire series. With the indication that this reaction can be prevented by proper fluid intake, together with appropriate alkali therapy, the total incidence of toxic reactions from sulfadiazine can be reduced to approximately 4 percent.

The authors feel that this study indicates a decided superiority of sulfadiazine over the commonly employed sulfonamides on the basis of low clinical toxicity.

## PATHOLOGY

**Pulmonary tuberculosis in paretic patients; its resemblance to clinical pulmonary syphilis.** Leonard Munson. *M. Bull. Vet. Admin., Washington*, 20: 305-312, Jan. 1944.

The Veterans' Administration has incorporated guiding standards for the diagnosis of syphilis of the lungs in *The Manual for Medical Examiners*. The coexistence of tuberculosis and syphilis in neuropsychiatric patients presents certain perplexities of diagnosis and therapy: (1) The Wassermann reaction in chronic pulmonary tuberculosis; (2) the identification and proper treatment of pulmonary tuberculosis complicating dementia paralytica; (3) the recognition of pulmonary syphilis in patients showing X-ray appearance of pulmonary tuberculosis, and in whom it is not possible to secure clinical evidence of the tubercle bacillus.

In the Veterans' Administration Facility, Northampton, there were 4 patients who had coexisting pulmonary tuberculosis and paretic dementia among the 38 patients in the ward. The author believes that the low incidence of less than 5 percent of pulmonary tuberculosis in paretic patients does not mean that paretic patients are relatively immune to pulmonary tuberculosis, but that it is due to the fact that the span of life for paretics is shorter than in other psychotic groups.

The diagnosis of pulmonary or extrapulmonary tuberculosis in a syphilitic patient should rest entirely on the finding of the tubercle bacillus. Because psychotic patients are for the most part deteriorated and uncooperative, it is often necessary to obtain specimens by means of early morning gavage. If the examination is negative, animal inoculation should be carried out, with concurrent spreads made from the stools, cultures of the sputum, stool and gavage specimens.

Five case reports are given at length. In the first case the diagnosis of pul-



monary tuberculosis was established before symptoms of central nervous system syphilis made their appearance. The chest condition progressed while the serologic tests became negative under treatment. In the second case a diagnosis of syphilis of the lung might have been made without animal inoculation of a gavage specimen, although serologic tests for syphilis were negative. There was excellent response to either antisyphilitic therapy, bed rest, or both. The third case also suggested that a therapeutic test is not specific for syphilis. In case 4 pulmonary tuberculosis and tertiary syphilis coexisted and probably had been present for a good many years. From the data in the fifth case, and according to accepted clinical standards, the patient might have had a diagnosis of syphilis of the lung. An extensive search revealed no tubercle bacillus and there was a definite history of syphilis and positive serologic reactions. There was distinct improvement under antisyphilitic therapy. However, after considering the similarity to the other 4 cases, a diagnosis of pulmonary fibrosis was made.

From the study of these cases, the author believes that the therapeutic test for syphilis of the lung is not specific; that in psychotic patients the animal inoculation of early morning gavage specimens is essential in establishing or eliminating the diagnosis of pulmonary tuberculosis. Accurate criteria for the antemortem diagnosis of syphilis of the lung are not available.

**Roentgen study of lymphogranuloma venereum: Report of twenty-four cases.** I. Klein. *Am. J. Roentgenol.*, Springfield, 51: 70-75, Jan. 1944.

Lymphogranuloma venereum of the colon has been studied in 24 cases. The findings in these cases are reported in a table, and the histories of 5 are summarized.

The symptoms of lymphogranuloma venereum, tenesmus, constipation, and mucous and bloody stools are caused by rectal strictures above the anal orifice and ulcerating and granulating tissue covering the entire rectum. Roentgen

studies show that in these cases there is a destruction of the mucosa, rectal strictures, distention of the rectal pouch, single and multiple perirectal and perisigmoid sinus formation, and fistulous tracts. Usually the roentgen picture of this disease is clear and of diagnostic value, as was illustrated in the cases studied by the author, of which some were negative for the Frei test and others were operated upon because of mistaken diagnosis.

The fact that lymphogranuloma venereum of the colon often assumes various forms occasionally leads to a mistaken diagnosis of cancer. However, one of the features of differentiation is the length of time the disease may run. Cases of lymphogranuloma venereum usually run a chronic course of 20 or more years, while cancer generally has a history of 2 or 3 years. In lymphogranuloma venereum, although the lesions may be localized, they more often circle the wall. These lesions begin in the anal region, while cancer tends to develop in the rectum.

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## LABORATORY RESEARCH

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**The sensitizing and indicator action of Victoria blue and Janus green on the flocculation reaction for syphilis.** F. M. Berger. *Brit. J. Exper. Path.*, London, 24: 252-260, Dec. 1943.

The influence of 78 different dyes on the flocculation test for syphilis was investigated. Certain dyes had no influence on the reaction, another group sensitized the reaction, and a third group, which included Janus green and Victoria blue, had both a sensitizing and an indicator action on the reaction. Syphilitic serums containing too little of the reacting substance to react with a suitable heart extract without dye showed marked flocculation in the presence of Victoria blue and Janus green. These dyes were also taken up by the precipitate, leaving a water-clear supernatant fluid.



The sensitivity of the reaction was a function of the amount of dye. Antigens containing dyes attained their full sensitivity immediately after dispersion, and maintained the same level of sensitivity for some time thereafter.

Making use of the sensitizing effect of Victoria blue, a simple and reliable slide flocculation test for the serologic diagnosis of syphilis was devised. This dye test was just as specific as, and somewhat more sensitive than, other commonly used serologic tests for syphilis, and the results were easy to read.

The sensitivity and specificity of the dye test was compared with that of Wyler's modification of the Wassermann reaction and Kahn's standard test on 1,112 serums. A table gives the results of the 3 tests. In all, 187 positive and doubtful serums were detected by the combined use of the tests; 26 serums reacted in the dye test but gave a negative result in the other two. A study of these 26 cases showed that the results given by the dye test were specific.

Although the dye test is somewhat more sensitive than the two tests used for comparison, it was not as sensitive as the collodion particles agglutination test (Berger, 1943). The dye test is, however, easier to perform, with very little laboratory equipment being required for its performance, and the stock antigen keeping indefinitely.

**The detoxication of neoarsphenamine by means of various organic acids.** E. W. McChesney, O. W. Barlow and G. H. Klinck, Jr. *J. Pharmacol. & Exper. Therap.*, Baltimore, 80: 81-92, Jan. 1944.

The authors made a further study on the detoxifying action of several organic acids, particularly ascorbic acid, on neoarsphenamine with a view toward explaining the mechanism and physiologic effects. The acids studied were ascorbic, isoascorbic, d-glucoscorbic, lactic, pyruvic, succinic, malic, mandelic, aspartic, gluconic, 2-ketogulonic and L-cysteine.

Experimental studies on albino rats show the toxicity of neoarsphenamine to be materially reduced by ascorbic, iso-

ascorbic, d-glucoscorbic and p-aminobenzoic acids. The effect is most favorable when the arsenical and the protective agent are injected intravenously in the same solution but the acids are somewhat effective if injected simultaneously at another site. However, the simultaneous injection of neoarsphenamine and ascorbic or isoascorbic acids resulted in no significant change in the excretion of arsenic, as compared to control animals injected with the arsenical only, nor was there any significant difference in the arsenic content of liver or kidney at various time intervals after the injection.

Ascorbic and p-aminobenzoic acids are of equal value as detoxicants for neoarsphenamine. If the detoxication of neoarsphenamine by means of organic acids is to be of value, it is necessary that the chemotherapeutic effect of the former should not be appreciably altered by the detoxicants. Sandground and Hamilton have shown that the trypanocidal action of carbarsone and arsanilic acid is not inhibited by p-aminobenzoic acid. The authors have found that the trypanocidal action of glyvarsenyl (3, 4'-diacetyl-amino 4-hydroxy-arsenobenzene 2'-glycolic acid) is not inhibited by the presence of 0.5 or 1 percent ascorbic or isoascorbic acid in the solution, nor is the trypanocidal action of neoarsphenamine inhibited by the simultaneous injection of ascorbic or isoascorbic acid at a level of 3 moles for each mole of neoarsphenamine. The function of the ascorbic acids appears to be primarily that of preventing oxidation, chiefly after injection.

**The pharmacologic basis for the widely varying toxicity of arsenicals.** Ralph B. Hogan and Harry Eagle. *J. Pharmacol. & Exper. Therap.*, Baltimore, 80: 93-113, Jan. 1944.

It is a possible corollary both of Ehrlich's general thesis and of the sulfhydryl theory that arsenicals may be active only to the degree that they are bound, and that the enormous differences in the toxicity of arsenic compounds may be due merely to their varying affinity for the body tissues. The present paper, based on experimental studies in rabbits, offers

further evidence that the toxicity of arsenic compounds is quantitatively a function of their affinity for tissue.

In a series of phenyl arsenoxides varying twentyfold in toxicity, the amount of each (acid-substituted compounds excepted) bound by red blood cells in vitro was in proportion to its systemic toxicity.

A similar variation was found in the amount of arsenical bound by the circulating red blood cells immediately after intravenous injection. The nontoxic compounds were not bound to the same degree as toxic compounds, and left the blood stream at a faster rate.

The amount of arsenic remaining in the liver and kidney 24 or 48 hours after the intravenous injection of arsenoxides or arsonic acids was proportional to their toxicity.

The rate of excretion of phenyl arsenoxides (acid-substituted compounds excepted) was also a function of their toxicity. The nontoxic compounds, not bound by body cells, were excreted rapidly; the toxic compounds were excreted slowly, in reverse proportion to their toxicity.

At dosages which produced equivalent toxic effects (the LD<sub>50</sub> level), trypanamide, phenyl arsonic acid, and phenyl arsenoxide resulted in comparable tissue levels, despite a 500-fold difference in absolute arsenic dosage.

It is therefore suggested that the varying systemic toxicity of arsenicals is primarily determined by the varying degree to which they are bound by, and thus block, essential functional groups in vital organs. The chemical nature of these groups is discussed in the text.

Acid-substituted phenyl arsenoxides are only an apparent exception to this generalization. Although fairly toxic, they were bound to only a minimal degree by red blood cells in vitro or in vivo. After intravenous injection, they were at first excreted rapidly, as much as 40 percent appearing in the urine in 1 hour. The excretion was, however, abruptly curtailed after approximately 4 hours, and death in white mice injected at the LD<sub>50</sub> level was characteristically delayed as compared with death resulting from other

phenyl arsenoxides. It seems probable that most acid-substituted phenyl arsenoxides are not toxic as such, consistent with their lack of affinity for red blood cells and their initially rapid excretion. The sudden curtailment of urinary excretion, and the delayed death of mice, suggest that they are converted by the body to other compounds which can combine with vital chemical groupings in the tissues, and which are toxic by virtue of that combination.

**Preservation of Wassermann sera by means of sulfanilamide.** James P. Crawford and Lucien D. Hertert. *Mil. Surgeon, Washington*, 93: 274-275, Sept. 1943.

Due to the high temperature of the remote desert regions a large number of badly contaminated serums have arrived at the laboratory of the Presidio of Monterey, California. It was believed that the sulfa group of drugs held some promise as a preservative inasmuch as a great many serums were being received that contained considerable amounts as a result of treatment.

Containers were prepared by pipetting 0.2 cc. of a 2 percent solution of sulfanilamide in 95 percent ethanol, into previously sterilized Wassermann tubes and drying with low heat. This process deposited 4 mg. of dry powder so finely granulated that it was highly soluble. This was not true of aqueous solutions. Drying is best done at temperatures below 80° C. to prevent charring of the chemical.

As a general rule from 1 to 3 cc. of serum were submitted by the stations for routine serologic tests. Kolmer and Kahn reactions have not been altered by the addition of 1.3, 2.0 or 4.0 mg. of sulfanilamide per cc. which were the concentrations achieved by adding the various amounts of serum (3, 2 and 1 cc.) to 4 mg. of the drug.

In observations involving over 3,000 serums in duplicate, no test has been altered sufficiently to change its reading either positive or negative. On the other hand, in several selected lots submitted from stations averaging 22 percent anti-complementary Wassermann reactions,



the number of untestable specimens was cut to 1.5 percent. This latter figure is probably due to causes other than bacterial contamination and is not reducible by the addition of a preservative. Positive and negative serums were held for 18 days at room temperature with no change of reaction and without becoming anticomplementary when sulfamilamide was added in a concentration of at least 1.3 mg. per cc.

**The influence of diet on sulfonamide action.** Esther M. Greisheimer, Roberta Hafkesbring and Grace E. Wertenberger. *Am. J. Digest. Dis.*, Fort Wayne, 11: 13-15, Jan. 1944.

Since their former publications, the authors have made further studies on the effects of diet on sulfonamide action, basing their data on the results found in 403 rats. Sodium salts of sulfadiazine and sulfapyrazine have been studied in addition to sodium salts of sulfathiazole and sulfapyridine.

The administration of sodium sulfathiazole to rats on the control diet caused a slight increase in blood sugar, while a more marked increase was seen in those on the high protein and the high carbohydrate diets. The high fat diet increased the susceptibility to some extent. A decrease in liver glycogen was seen in every case, being most marked on the control diet.

The administration of sodium sulfadiazine showed a very slight effect on the blood sugar, regardless of the diet. So far as liver glycogen was concerned, the high protein diet offered the least and the high carbohydrate the most protection against the drug action. The blood levels were highest after administration of this drug.

Sodium sulfapyridine had the most pronounced effect on both blood sugar and liver glycogen in animals on every diet. The high fat diet seemed to render the animal particularly susceptible to the action of the drug on blood sugar. The decrease in liver glycogen was greatest on the control diet. These findings are in accordance with those already reported by the authors. The drug concentrations

were maintained at approximately the same levels on every diet, and the greatest conjugation occurred on the high protein diet.

Sodium sulfapyrazine showed an increase in blood sugar in every diet, more marked in rats on the high carbohydrate diet and least in those on the control diet. The decrease in liver glycogen was constant in animals on the control, the high fat and the high protein diets, but an increase was found in those on the high carbohydrate diet. This drug was like sodium sulfadiazine in that the blood level remained high and its effect on liver glycogen was similar. Unlike sodium sulfadiazine, it did affect the blood sugar.

Sodium sulfadiazine with a high carbohydrate diet seemed preferable if changes in carbohydrate metabolism were to be avoided.

**Value and shortcomings of the cultural method in the diagnosis of gonorrhea: With special reference to the use of the Peizer medium.** Mason Trowbridge, Jr., and Ruth M. McConkey. *War Med.*, Chicago, 5: 36-42, Jan. 1944.

In order to determine the relative merits of the Peizer medium with nile blue A and chocolate agar (Difco) in the culture of gonococci, 128 pairs of Peizer and chocolate agar plates were inoculated with the same material. The material used was from a few female patients, from males being tested for cure, from patients with chronic urethritis, and gonococci from pus or primary cultures which were mixed with contaminants before inoculation on the plate.

Of the 128 pairs of plates, 84 did not yield a growth of gonococci on either medium. In most instances the chocolate agar supported a heavy growth of contaminants and the Peizer medium did not. For purposes of comparison each plate was marked by two examiners. "Very good" signified numerous discrete colonies of gonococci; "good," few isolated colonies and a moderate growth of contaminants; "fair," colonies of gonococci intimately mixed with contaminants, and "poor," few colonies of gonococci almost overgrown with contami-



nants. The results of the experiment with chocolate agar and Peizer medium, respectively, were: very good, 1 and 17; good, 5 and 18; fair, 17 and 6; poor, 12 and 2; failure, 9 and 1.

The authors feel that the superiority of the Peizer medium to the chocolate agar has been demonstrated.

However, both mediums are still far from perfect, as has been shown in several instances where both plates were inoculated with a mixture of known viable gonococci and other organisms and the gonococci were overgrown by contaminants. Gonococci sometimes grow better on chocolate agar in the presence of contaminants than alone.

The cultivation of gonococci is a valuable laboratory procedure when done by experienced laboratory workers. The Peizer medium is recommended for use in Army hospitals until a better medium is introduced.

The authors describe in detail the preparation of the Peizer medium, together with certain steps in the cultivation and identification of the gonococci.

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## **PUBLIC HEALTH ADMINISTRATION**

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**Law enforcement for social protection—a health measure.** Eliot Ness. Wisconsin M. J., Madison, 43: 235-237, Feb. 1944.

Since its formation in 1941, the Social Protection Division of the Federal Security Agency has been instrumental in bringing about the closing of segregated red light districts in practically every town and city near a military camp or a war industrial center. The Division has been particularly helpful in securing the cooperation of hotels, rooming houses, bars, taverns, and taxicab companies by developing their own self-policing methods to eliminate prostitution and promiscuity from their own businesses or premises.

The responsibilities for promoting a unified program of venereal disease control

rest upon the cooperation of such agencies as the United States Public Health Service, the Social Protection Division of the Federal Security Agency, the Army and the Navy, and the American Social Hygiene Association. The actual work is done by the States and communities under the leadership of the State health departments. It is being accomplished through the work of the police officer, the facilities of State and local health departments and the private physicians, the services of welfare and social agencies, and the cooperation and understanding of parents and citizens.

### **Genitoinfectious disease as a measure of sexual promiscuity in a community.**

N. A. Nelson. Monthly Bull., Maryland State Dept. of Health, Baltimore, 15: 93-97, Feb. 1944.

In 1936, as a result of Surgeon General Parran's article "Why Don't We Stamp Out Syphilis?" and the public demand, the health officer was again forced to consider genitoinfectious disease control, after a lapse in activities for several years. He emphasized that syphilis and gonorrhea were public health, not moral or sex, problems. The author believes, however, that it is not sound policy to continue to ignore the basic epidemiologic fact that syphilis and gonorrhea are spread as a result of sexual promiscuity. He says that it is like trying to control typhoid fever while ignoring the cleaning up of the water supplies.

The prevalence rate of syphilis and gonorrhea in a community is directly proportional to the degree of promiscuity. Some population groups are far more promiscuous than others; the Negro, as a race, is far more promiscuous than the white, and has a far higher rate of infection. Prostitutes are the most efficiently promiscuous part of the population, and they are effective spreaders of disease.

Lack of normal and familiar facilities for entertainment contributes to an increase in sexual activity among those away from home in the Armed Forces or in war industries, and while the rate of sexual contact may be the same as

"back home," it is probably far more promiscuous.

Back home, the sexual contacts were probably restricted to regular partners; in the new environment, a new sexual partner for each experience adds to the total of promiscuity. Under such conditions it is difficult to catch up with disease through epidemiologic investigation.

Some States, notably the New England States and Wisconsin, have been able to bring syphilis more nearly under control because sexual promiscuity has been reduced to the point where public health procedures prevent infections faster than the reduced promiscuity can produce them.

The author does not wish to say that health departments should close their clinics and stop trying to control genito-infectious disease. In trying to control other infectious diseases, as tuberculosis and typhoid fever, the health officer uses every means at hand to keep rates from going higher. Likewise, he owes it to the community to make it clear that as long as sexual promiscuity is the order of the day, venereal diseases cannot be expected to be eliminated.

**Why youth should know the important facts about venereal diseases.** Maurice A. Bigelow. *J. Social Hyg.*, New York, 29: 612-613, Dec. 1943.

The author submits 4 points for consideration in the teaching of the important facts about venereal diseases in high schools and colleges. They are:

(1) Scientific information concerning the causes and effects of syphilis and gonorrhea prevents infection of some young persons who without such knowledge might become infected.

(2) Scientific information as to the dangers of going without medical treatment or of attempted self-treatment leads many persons to seek medical advice and treatment promptly, and to persist until treatment is adequate.

(3) Positive information concerning social and public health relations of venereal diseases leads many citizens to support laws and education looking toward their

control. This result of health education of the public and in schools is building permanent foundations for public health movement, and this is especially true as applied to venereal disease control education.

(4) Scientific teaching, without dramatics, will tend to counteract some of the exaggeration which has appeared in overpopularized leaflets, newspapers, talks and pictures. Exaggeration and misleading dramatic handling of facts and especially figures may in the long run lead to loss of interest and support when the public learns the real facts.

Sexual conduct is determined by ethical attitudes and standards more than by knowledge of scientific facts. In view of this truth, many public health leaders in the venereal disease campaign maintain that in the home, school, church, and youth-guiding agencies there should be more education that aims to develop character or standards of conduct in the relations between the sexes.

**Canada's first National Venereal Disease Control Conference.** D. H. Williams, *Canad. M. A. J.*, Montreal, 50: 157-158, Feb. 1944.

On July 1, 1943, a comprehensive venereal disease control program was launched in Canada. This program was initiated by the Army and included the control measures of Navy, Air Force, Department of Pensions and National Health, and Provincial Health Departments. To further enlist the cooperation of all interested agencies in Canada, a National Venereal Disease Control Conference was held in Ottawa in December 1943. Delegates and visitors from the entire United Kingdom and the United States were present. The purpose of the conference was to consider how the existing administrative facilities for the prevention of venereal disease could best be utilized and what need existed for modification and extension of these facilities.

The four-sector front against venereal diseases had been adopted—health, welfare, legal and moral sectors. To this was added at the National Conference the adoption of a six-point strategy on the



health sector, which includes health education, medical care, abolition of quackery, prenatal blood tests, premarital blood tests, and contact investigation.

**New decree in Rumania regarding venereal disease.** Brit. M. J., London, No. 4336: 217, Feb. 12, 1944.

"A new decree has been issued in Rumania which states that everyone with venereal disease must undergo treatment, and premarital certification of freedom from infection is obligatory. Physicians must report defaulting patients. Persons exposed to risk through their profession—e. g., those serving in hotels, restaurants, night clubs, public baths, as well as peddlers and street vendors—are subject to periodic examinations. Correctional imprisonment of 1 to 3 years is imposed on clandestine prostitutes and proprietors of hotels who allow prostitution on their premises. Knowing transmission of the disease to others carries a sentence of 1 to 5 years' correctional imprisonment and a fine of 50,000 to 200,000 lei. \* \* \* Persons undergoing medical treatment at the time of transmission of the disease will be severely punished without the application of extenuating circumstances. Free blood tests are made by the State. Brothels are again permitted by law."

**Health in Hartford, 1941-42.** 57th and 58th Annual Reports of the Board of Health, Hartford, 30-43, 1943.

During 1941-42, Hartford's draft boards reported 126 persons whose serologic tests for syphilis were positive, and 13 with positive tests for gonorrhea. The procedure is to send a transcript of his record with the inductee when he leaves for the reception center, thus assisting the Army in procuring this necessary information.

Several large industries in Hartford have included routine blood tests in pre-employment examinations. In one local war industry 15,172 examinations were made during 1941, and 121 persons were found to be infected with syphilis. This is 0.87 percent of the number examined and 2.5 percent of the physical defects found. These persons are not refused em-

ployment but are required to present to the medical department of the company each month a written statement that they are under treatment.

A series of tables show the result of the compilation of data from reports received by the Bureau.

**Venereal disease control in Florida 1944.**

R. F. Sondag. Florida Health Notes, Jacksonville, 36: 21-48, Feb. 1944.

The author reports on the activities of the Division of Venereal Disease Control of Florida for the year 1943, with some comparative reports for previous years.

Through December 1943, of 292,157 selectees examined, 40,810 were found positive. The rate for Negroes was 287.1 per 1,000 and for white 36.7, the total rate being 139.7.

The prevalence of syphilis in selectees tested in Florida through November 1943 for white, Negro, and combined rates per 1,000 by counties is shown in three maps. A graph and a table showing the number of new cases of syphilis and gonorrhea reported from 1934 to 1943 are given.

For 1943, 33,601 new cases of syphilis and 16,957 of gonorrhea were reported. These new cases were discovered by means of Selective Service examinations, blood tests made on all health card applicants, and the epidemiologic activities of 34 follow-up case workers. There were 844 new cases of chancroid, 251 of granuloma inguinale, 254 of lymphogranuloma venereum, and 23 of ophthalmia neonatorum, which was an increase over 1942.

Thirteen additional clinics were established during the year. A table shows the marked increase in the amount of free drugs distributed in the State.

From March through December 1943, a total of 1,077 girls was released from Wakulla and Ocala quarantine hospitals, which employed either the 5-day drip or the Eagle method of intensive treatment. Of these, 65.7 percent were white and 34.3 percent Negro; 41.5 percent were under 19 years of age and 76.6 percent were under 24. Of these patients, 28 percent had a combination of venereal diseases, 0.6 percent had granuloma inguinale, lymphogranuloma venereum or chancroid alone,



16 percent had syphilis alone, and 42 percent had gonorrhea alone. Seventy-four percent were discharged as cured, and there were 2.6 percent readmissions during this period. Analyses of these 1,077 girls are given in 6 tables. A different type of intensive treatment is being employed at a rapid treatment center in Jacksonville, and after further evaluation a report will be made on it.

A general outline of the plans for a State-wide educational program to be launched Jan. 1, 1944 is given. The Division of Venereal Disease Control has solicited the aid of every agency, club and organization. The Governor of Florida has been most cooperative in this program.

**Pinta in Venezuela.** (El carate en Venezuela.) D. R. Iriarte. *Rev. de med. trop. y parasitol., bacteriol., clin. y lab.*, Havana, 8: 75-81 and 9: 1-7, Nov.-Dec. 1942 and Jan.-Feb. 1943. Abs. in *Trop. Dis. Bull.*, London, 41: 66-67, Jan. 1944.

The author discusses the origin of pinta or carate and its incidence in Venezuela. In several sections of the country the incidence of this disease is more than 50 percent, while the average for the whole State is 10 percent. The article deals with the etiology, transmission, age and sex prevalence and differential diagnosis of the disease. The distinguishing features between white pinta and vitiligo are especially pointed out.

A brief description of the prognosis, relapse, reinfection and immunity, prophylaxis and treatment is given. Reinfections may occur. The prognosis is not very favorable. Treatment consists of arsenicals at the beginning, followed by bismuth.

The author has observed 281 patients.

**What is "Sex Education"?** Ray H. Everett. *J. Social Hyg.*, New York, 29: 614-619, Dec. 1943.

The author, at the request of the Washington Evening Star, prepared an article on "What is Sex Education?" This article was published on May 1, 1943 during the course of a lively public discussion by the District of Columbia Board of Edu-

cation as to whether social hygiene instruction should be expanded in the public schools of Washington, and if so, what should be taught. The Board decided in favor of this action by incorporating into the curriculum, Unit 10—Human Reproduction. An outline of the course as approved by the Board of Education is given. Educators to whom the outline has been shown agree that it is an excellent and comprehensive charter for instruction in this field and that it presents challenging opportunities for the teaching staff.

There are five great tasks for this type of education: (1) Developing an open-minded, serious, scientific, and respectful attitude toward all problems of human life which relate to sex. (2) Giving that knowledge of personal sex hygiene which makes for the healthful and efficient life of the individual. (3) Developing personal responsibility regarding the social (including ethical) and eugenic aspects of sex as affecting the individual life in its relation to other individuals of the present and future generations—in short, the problems of sex instinct and actions in relation to society. (4) Developing an appreciation and understanding of family life. (5) Teaching very briefly, during adolescence, the essential hygienic and social facts regarding the destructive venereal diseases and dealing with them as with other communicable diseases in college hygiene and in lectures to adults.

The author stresses that the home is the logical place for most social hygiene training; but until parents are better qualified for such teaching than they are at present, the schools have a duty to perform which they cannot ignore.

**Ophthalmia neonatorum.** *Lancet*, London, 2: 645, Nov. 20, 1943.

At the meeting of the Royal Society of Medicine on Nov. 9, 1943, Professor Arnold Sorsby reported that annual returns from the Ministry of Health showed that for the 7 years, 1934-40, 44 children were blinded from ophthalmia neonatorum; during 1941-42 only one case was reported. The incidence of impaired vision has likewise declined, the figures for the

two periods being 190 and 14, respectively. It is likely that the improvement is due largely to sulfonamide therapy.

Blindness from ophthalmia neonatorum has been diminishing steadily throughout the present century. During 1907-13 it constituted 18.0 percent of all causes of blindness in children admitted to the London County Council blind schools, and had declined to 11.9 percent during 1914-20. In 1931, 21.1 percent of the children at these schools were blind from this disease; by 1938 the proportion had fallen to 14.0 percent, and in 1943 it was 9.8 percent. However, Sorsby stressed that blindness from ophthalmia neonatorum is still to be reckoned with; it was the cause of blindness in at least 15 out of the 127 infants under 5 years of age at the Sunshine Homes of the National Institute for the Blind.

As yet there is no standard prophylaxis in ophthalmia neonatorum. Emphasizing the paramount importance of adequate

antenatal care, Sorsby reported that data from the larger lying-in centers indicated that the incidence of gonococcic ophthalmia was no less at centers using silver nitrate than at those using organic silver. In 70,386 births at which silver nitrate had been used, 64 cases of gonococcic ophthalmia had occurred, while in 39,432 births at which protargol was used, there were 21. On the other hand, in Scotland, where silver nitrate is recommended for routine use by the Scottish Central Midwives Board, the incidence of blindness from ophthalmia neonatorum is distinctly lower than in England and Wales (0.23 against 1.25 for 100,000 births during 1934-38).

A report on 500 patients with ophthalmia neonatorum treated at White Oak since January 1940 makes it clear "that in the sulfonamides we have a therapeutic agent which makes blindness or impaired vision from this affection no longer tolerable."



# New Cases of Syphilis and Gonorrhea in States, Territories, and Possessions

Health officers' monthly statement: Reported for the first 7 months of fiscal years 1943-44 and 1942-43

Area	Cases of syphilis and gonorrhea reported for first 7 months of fiscal years below											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital			
	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43
United States†	264, 277	326, 503	44, 368	47, 539	70, 730	84, 292	114, 618	146, 078	7, 603	9, 118	169, 500	156, 457
Alabama-----	10, 157	12, 716	1, 448	1, 650	2, 338	3, 473	2, 446	3, 886	219	322	3, 848	5, 489
Arizona-----	1, 653	1, 219	392	169	442	237	643	713	71	45	1, 038	460
Arkansas-----	5, 759	9, 598	703	1, 067	1, 932	3, 619	2, 191	3, 906	134	149	2, 651	2, 898
California-----	18, 401	17, 405	3, 041	2, 412	4, 339	3, 773	10, 115	10, 039	553	479	19, 503	13, 233
Colorado-----	2, 520	2, 594	609	478	713	582	1, 096	1, 421	102	113	1, 993	1, 301
Connecticut-----	1, 727	1, 599	213	157	710	455	480	590	71	62	910	859
Delaware-----	529	561	61	76	128	130	107	169	8	16	112	108
Dist. Columbia--	4, 663	(*)	543	(*)	1, 127	(*)	2, 770	(*)	81	(*)	2, 147	(*)
Florida-----	17, 085	19, 992	1, 926	2, 524	5, 327	4, 830	7, 775	10, 087	346	443	9, 813	7, 588
Georgia-----	9, 320	16, 679	1, 838	2, 321	3, 726	7, 731	3, 484	6, 175	268	451	6, 277	7, 739
Idaho-----	338	262	160	90	59	17	93	117	5	15	503	154
Illinois-----	16, 212	17, 437	2, 126	1, 962	3, 755	3, 473	10, 019	11, 567	312	435	13, 702	11, 914
Indiana-----	4, 943	8, 295	743	1, 042	460	163	1, 799	3, 173	134	281	2, 030	2, 657
Iowa-----	1, 417	1, 710	285	186	367	565	612	767	98	63	1, 055	1, 049
Kansas-----	1, 618	2, 328	335	472	325	224	896	1, 055	62	67	1, 135	1, 558
Kentucky-----	4, 202	8, 136	618	955	915	1, 647	1, 794	3, 515	171	252	2, 076	2, 714
Louisiana-----	10, 762	11, 472	1, 747	1, 542	2, 796	3, 279	2, 820	5, 553	274	336	7, 996	3, 578
Maine-----	(*)	531	(*)	123	(*)	79	(*)	238	(*)	60	(*)	414
Maryland-----	9, 172	10, 281	987	724	937	850	1, 629	1, 202	72	127	4, 461	4, 683
Massachusetts--	3, 269	3, 275	670	555	§	§	2, 404	2, 563	193	155	2, 968	2, 750
Michigan-----	9, 945	7, 918	1, 445	1, 091	2, 583	1, 660	4, 193	3, 489	254	302	6, 450	5, 308
Minnesota-----	1, 418	1, 832	134	130	139	191	1, 051	1, 407	64	65	1, 141	909
Mississippi-----	15, 191	23, 941	5, 156	5, 955	4, 279	8, 076	5, 147	9, 026	605	884	17, 410	19, 591
Missouri-----	6, 001	6, 197	1, 033	955	1, 545	1, 261	2, 869	2, 980	197	167	3, 345	2, 708
Montana-----	242	312	66	102	41	21	98	147	5	5	192	192
Nebraska-----	749	1, 295	117	139	368	301	210	785	23	39	903	1, 066
Nevada-----	450	504	15	(*)	81	(*)	312	(*)	17	(*)	227	164
New Hampshire---	139	185	18	20	32	16	77	123	6	17	115	120
New Jersey-----	6, 476	6, 733	775	802	2, 019	1, 688	3, 403	3, 937	263	235	3, 132	4, 109
New Mexico-----	1, 142	1, 160	245	212	259	246	582	622	56	62	843	376
New York-----	21, 726	21, 454	3, 231	2, 073	3, 721	3, 395	13, 895	15, 600	609	738	11, 451	9, 216
North Carolina--	6, 580	10, 757	1, 700	2, 207	2, 641	4, 406	2, 124	3, 851	115	293	5, 273	6, 392
North Dakota---	175	212	61	28	29	34	51	94	10	12	160	163
Ohio-----	13, 371	13, 749	2, 061	1, 925	3, 174	3, 142	6, 820	8, 080	535	602	3, 103	2, 809
Oklahoma-----	4, 632	6, 135	607	918	1, 326	2, 337	1, 708	1, 500	172	161	2, 927	2, 668
Oregon-----	1, 206	894	364	163	99	85	707	572	36	57	1, 518	742
Pennsylvania---	7, 743	3, 094	1, 023	648	2, 983	2, 079	2, 824	19	385	32	614	(*)
Rhode Island---	643	714	48	27	68	56	463	548	15	25	444	300
South Carolina--	8, 308	11, 943	1, 853	2, 395	3, 312	4, 945	2, 729	4, 180	198	275	3, 478	3, 396
South Dakota---	282	278	58	47	42	113	134	98	25	11	239	177
Tennessee-----	10, 879	14, 434	1, 435	1, 771	4, 433	4, 707	4, 668	7, 469	242	336	8, 810	6, 467
Texas-----	15, 034	31, 167	1, 819	3, 384	4, 509	5, 935	6, 156	9, 577	424	634	6, 370	11, 312
Utah-----	530	362	134	115	71	44	313	194	12	8	380	489
Vermont-----	150	156	51	82	43	0	49	67	7	7	109	114
Virginia-----	8, 616	11, 219	2, 478	3, 259	3, 281	3, 916	2, 560	3, 643	163	219	7, 327	4, 786
Washington-----	2, 619	(*)	532	(*)	577	(*)	1, 148	(*)	83	(*)	5, 225	(*)
West Virginia---	2, 212	3, 423	396	511	353	581	533	977	66	110	1, 331	1, 441
Wisconsin-----	558	631	105	122	0	1	447	499	6	10	647	488
Wyoming-----	795	245	63	76	111	8	404	96	17	1	104	222
Territories and possessions												
Alaska-----	58	106	32	21	13	31	10	28	1	5	266	325
Hawaii-----	506	676	92	207	63	77	363	318	27	31	974	899
Puerto Rico-----	9, 287	5, 472	964	1, 212	1, 886	814	3, 053	1, 917	1, 166	984	2, 385	1, 823
Virgin Islands--	127	133	25	33	76	74	20	20	6	6	211	82
Actual total of United States, Territories, possessions†	281, 537	333, 421	46, 571	49, 135	74, 553	85, 367	122, 294	148, 599	8, 984	10, 204	181, 322	160, 000

\*Data not available.

\*\*Includes "Not stated."

†Based on States reporting in both fiscal periods.

‡Includes all reported cases.

§Included in late and late latent.

<sup>1</sup> Based on 46 States.

<sup>2</sup> Based on 45 States.

# New Cases of Syphilis and Gonorrhea in Cities of 200,000 Population and Over

Health officers' monthly statement: Reported for the first 7 months of the fiscal years 1943-44 and 1942-43

City	Cases of syphilis and gonorrhea reported for first 7 months of fiscal years below											
	Syphilis										Gonorrhea	
	Total **		Primary and secondary		Early latent		Late and latent		Congenital			
	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43
Total †.....	<sup>1</sup> 85,210	<sup>1</sup> 86,151	<sup>2</sup> 10,557	<sup>2</sup> 9,665	<sup>3</sup> 19,771	<sup>3</sup> 16,777	<sup>4</sup> 38,165	<sup>4</sup> 43,795	<sup>3</sup> 1,664	<sup>3</sup> 1,922	<sup>1</sup> 44,628	<sup>1</sup> 39,580
Akron.....	532	775	72	109	133	154	298	477	29	35	204	151
Atlanta.....	1,613	2,280	423	563	508	769	774	934	19	14	760	548
Baltimore.....	7,349	7,838	760	520	673	542	1,266	859	40	40	1,744	2,198
Birmingham.....	2,750	3,939	193	363	799	1,150	700	975	51	111	369	603
Boston.....	1,061	1,229	210	181	0	147	682	798	29	44	772	710
Buffalo.....	1,198	1,120	143	95	141	19	883	962	31	44	521	553
Chicago.....	9,020	10,324	1,430	1,393	2,162	2,055	5,258	6,601	170	275	7,660	7,867
Cincinnati.....	1,839	2,109	244	226	(*)	(*)	(*)	(*)	(*)	(*)	566	616
Cleveland.....	2,359	2,204	437	377	752	506	1,113	1,251	57	70	858	896
Columbus.....	874	897	174	105	189	186	467	574	24	32	182	262
Dallas.....	1,472	2,065	266	247	303	316	892	1,483	10	19	437	701
Dayton.....	1,038	737	118	112	295	131	592	465	33	25	433	176
Denver.....	1,228	1,281	275	226	318	207	464	800	38	32	1,092	614
Detroit.....	7,014	4,886	905	644	2,172	1,221	3,816	2,916	121	105	3,401	2,935
Honolulu.....	261	422	40	176	37	54	165	171	19	21	667	718
Houston.....	1,123	2,623	183	194	395	965	511	1,385	34	79	1,331	590
Indianapolis.....	(*)	2,486	(*)	350	(*)	60	(*)	633	(*)	26	(*)	369
Jersey City.....	308	453	31	37	65	69	204	330	18	17	27	34
Kansas City.....	1,058	1,257	178	187	194	160	644	784	40	55	564	508
Los Angeles.....	6,531	4,809	0	90	2,629	1,637	3,724	2,949	178	133	2,917	2,812
Louisville.....	1,232	1,765	189	189	217	308	517	1,061	13	39	518	801
Memphis.....	3,881	4,614	328	376	1,842	1,600	1,656	2,558	55	50	3,298	1,459
Milwaukee.....	291	312	30	48	4	0	243	258	1	6	107	79
Minneapolis.....	398	506	62	54	61	85	265	363	8	13	474	419
Newark.....	1,347	1,530	168	195	349	389	789	914	41	32	521	654
New Orleans.....	(*)	2,202	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	603
New York.....	15,031	15,555	2,688	2,015	3,329	2,764	8,464	9,808	369	420	8,199	6,560
Oakland.....	919	722	104	80	225	166	554	439	26	19	793	519
Oklahoma City.....	1,191	1,116	116	159	329	360	380	361	23	17	559	460
Omaha.....	335	670	30	68	189	134	91	436	18	21	297	489
Philadelphia.....	5,955	1,765	203	194	716	9	(*)	1,422	52	18	534	91
Pittsburgh.....	(*)	4,755	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	117
Portland.....	523	462	137	86	33	29	345	321	8	27	601	378
Providence.....	(*)	341	(*)	18	(*)	26	(*)	271	(*)	8	(*)	88
Rochester.....	157	191	31	14	13	1	110	169	3	7	173	130
St. Louis.....	(*)	2,887	(*)	364	(*)	880	(*)	1,558	(*)	85	(*)	723
St. Paul.....	173	313	20	30	30	40	111	225	5	9	178	119
San Antonio.....	697	933	93	82	191	232	384	563	24	41	816	582
San Diego.....	724	646	67	73	210	208	392	356	26	8	533	433
San Francisco.....	1,751	2,145	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	1,273	1,951
Seattle.....	808	768	103	100	143	99	510	513	14	12	979	781
Syracuse.....	605	485	17	16	20	1	551	457	17	11	190	77
Toledo.....	564	405	89	41	105	64	350	279	20	21	80	106
Washington, D. C.....	4,663	(*)	543	(*)	1,127	(*)	2,770	(*)	81	(*)	2,147	(*)
Actual total †.....	89,873	98,822	11,100	10,397	20,898	17,743	40,935	47,679	1,745	2,041	46,775	41,480

\*Data not available.

\*\*Includes "Not Stated."

†Based on cities reporting in both fiscal periods.

‡Includes all reported cases.

<sup>1</sup> Based on 38 cities.

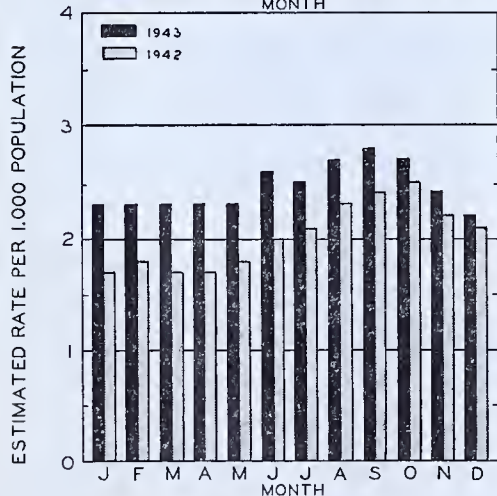
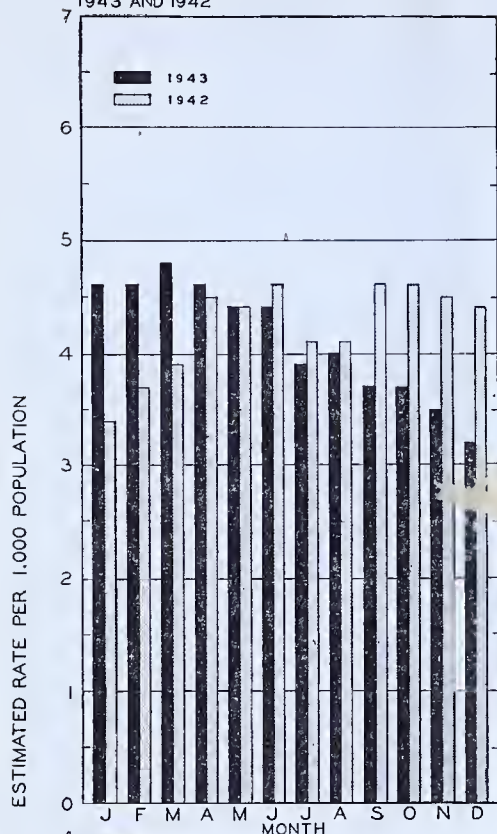
<sup>2</sup> Based on 37 cities.

<sup>3</sup> Based on 36 cities.

<sup>4</sup> Based on 35 cities.

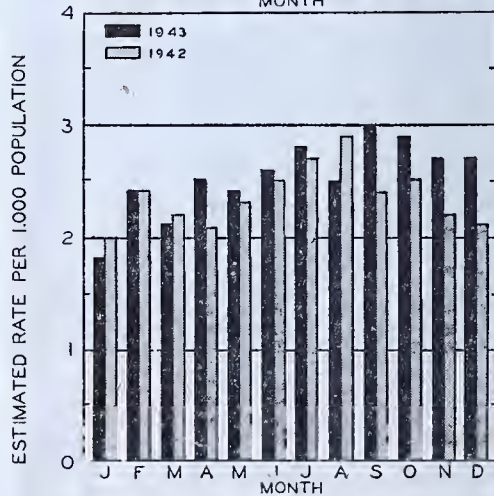
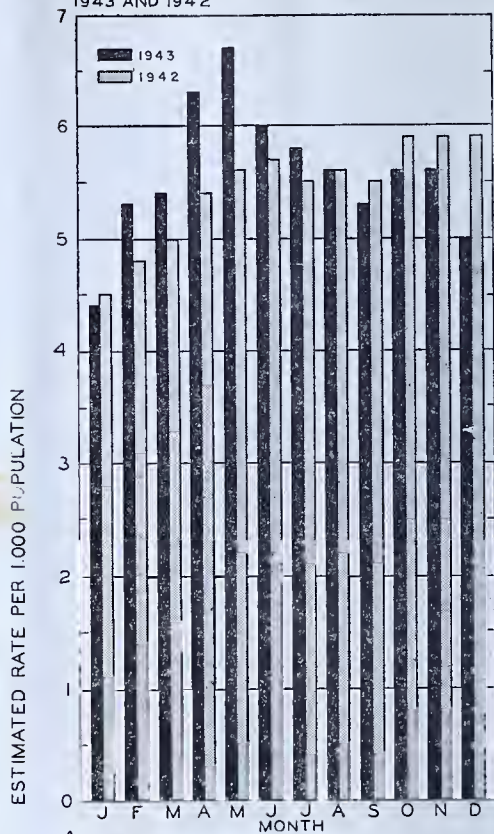


ANNUAL SYPHILIS CASE RATES  
IN THE UNITED STATES  
BASED ON PROVISIONAL MONTHLY DATA  
1943 AND 1942



ANNUAL GONORRHEA CASE RATES  
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ANNUAL SYPHILIS CASE RATES  
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# Venereal Disease Information

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FEDERAL SECURITY AGENCY  
UNITED STATES PUBLIC HEALTH SERVICE  
THOMAS PARRAN, *Surgeon General*

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# Trichomonas Urethritis and Prostatitis: A Preliminary Report on Incidence and an Analysis of 44 Cases of this Common Venereal Infection

Russell B. Roth, M. D.

Since the earliest descriptions of the occurrence of *Trichomonas vaginalis* in the male genito-urinary tract (Miura, 1893; Marchand, 1894; Dock, 1896) there has been a persistent though small accumulation of literature on the subject. Single case reports or studies constitute the majority of the papers so that, writing in 1941, Baumeister and Hollinger reached a figure of 145 reported cases, plus a somewhat indefinite series of approximately 23 cases reported by Riba and Harrison. The inference has been that the disease is uncommon; the primary purpose of this report is to show that it is not.

Interest in the disease has received most of its impetus from gynecologists who, discouraged by the high recurrence rate in their female patients, have investigated the sexual partners as a possible source. A few investigations have been made to establish its incidence in the so-called "nonspecific urethritis." No figure is to be found in the literature which gives an adequate expression of the incidence of infestation in the general population. The present work was done to determine such a figure. The study disclosed such an unexpected wealth of case material that it has been decided to expand the scope of the investigations into a more complete evaluation of all phases of the problem. It seems advisable, however, to give a preliminary report of the initial findings in the hope of stimulating a more widespread interest in, and recognition of the disease.

## ETIOLOGY

The parasite, first described by Donné (1836), has become familiar to all physicians dealing with leukorrheal discharges in women. There has been much discussion over the differentiation of species. Numerous varieties of this unicellular flagellate have been described, but the weight of evidence from morphologic studies, as well as inoculation from the James Buchanan Brady Urological Institute, Johns Hopkins Hospital, Baltimore.

experiments in apes and human subjects, seems to favor the existence of three major and distinct varieties which are of importance in the human being. These are: *T. hominis*, a denizen of the lower alimentary tract; *T. buccalis*, which is found in the mouth, and *T. vaginalis*, which occurs in the urogenital passages. *T. vaginalis* is the only one reported as occurring in the urogenital passages, and it has been the only one encountered in the present studies.

## INCIDENCE

Wide variance is to be found in estimates of incidence in the female, but an average figure of reported studies would be somewhere between 40 and 60 percent. Few figures of any kind for infestation in the male are available. Hogue examined 633 urine sediments by wet spread and cultural methods and found the parasite only once. Stuhler found *T. vaginalis* reported only 16 times in 32,000 examinations of prostatic secretion. Liston and Lees found 16 cases in 400 consecutive cases in their venereal disease clinic. Nitschke found that 12.5 percent of 40 cases of nonspecific urethritis showed *T. vaginalis*. Karnaky examined 150 sexual partners of infested women and found 38 cases.

The material for the present study consisted of unselected male hospital patients on the medical and surgical services of the Johns Hopkins Hospital. Age played no part, except that in the group under consideration there were no pre-adolescent boys. All patients with sufficient intelligence and cooperation to void according to directions were utilized, without regard for medical or surgical reason for hospitalization. Cases found in the initial survey were subjected to a thorough investigation to evaluate symptoms, extent of infestation, and, in some cases, response to therapy.

To date 62 Negro males have been examined, with the discovery of 17 infes-

tations, and 100 white males, with the discovery of 4 cases. It is believed that, whereas the incidence of 27.4 percent in Negro males may be accepted as a fairly reliable figure, a larger series must be run among white males before the figure can be definitely established. This portion of the investigation, therefore, yielded 21 cases for study among patients already hospitalized for some other reason. Twenty-three additional cases are analyzed in this report, most of which were found in the urologic outpatient department of the Johns Hopkins Hospital. It is quite apparent that to rapidly increase the size of a series for study it is only necessary to examine more of the dispensary class of Negro males.

#### DIAGNOSIS

Much has been written on the identification of the parasites by examination of wet spreads, stained spreads, and by cultural technics. In the present study reliance has been placed entirely on the wet spread technic which is described. Occasionally cultures were found to be negative in known positive cases, and for this reason have not been used. It may be mentioned, however, that use of the media described by Boeck and Drbohlav for cultivation of intestinal amebas has been generally satisfactory. The use of the stained spread has been discarded for routine study because it does not lend itself to immediate identification of the parasite while the patient is still in the clinic, and has not yielded a higher percentage of positives than the method here described.

Preparation is made for a routine three-glass urine test. In the first glass a common 15 cc. centrifuge tube is placed. The patient is instructed to void in a continuous stream while the examiner moves the glasses. Cleaning the glans is omitted, and in the uncircumcised patient the foreskin is left forward by preference. The first portion of the urinary stream is caught in the centrifuge tube, and as the stream continues the glasses are manipulated as in the ordinary three-glass test. The centrifuge tube is then spun for approximately 1 minute at a low rate of revolution, and the urine emptied out. The tube is then tapped against a table

top to stir up the sediment in the few remaining drops of liquid, and 1 drop of this material is placed on a clean glass slide and covered with an ordinary coverslip. The specimen is promptly examined under the low power of the microscope. With very little practice parasites are quite readily identified by their characteristic motility. Identification is confirmed by shifting to high power. In the present series, identification has been further checked by stained spreads, and in some cases with cultures to exclude the possibility of encountering other flagellate than *T. vaginalis*.

When the described technic is followed the diagnosis of *T. vaginalis* infestation proves simple and reliable. No more elaborate procedures appear necessary. It is to be pointed out, however, that its virtue is annulled by any prevention of prompt and careful investigation of the specimen. Whereas flagellate motility in such specimens has been observed for over 4 hours, it is only during the first 5 or 10 minutes that the parasites regularly indulge in the random free-swimming motility which makes them relatively easy to locate under low power. If examination is postponed the organisms frequently require a patient and tedious search under higher power magnification. In these cases they usually are firmly anchored to some bit of detritus by their axostyles, and only a brief jerk of the cell body is visible with each lashing of the flagella. The motion of the undulating membrane also persists but cannot be readily appreciated under low power. Any attempt to hurry the search of the slide will reduce the number of positives. In a large majority of cases identification in positive cases is made in a few seconds. An occasional specimen will be found positive only after a longer search. The presence of numerous desquamated epithelial cells in a specimen is reason for careful search since there is a high correlation between the appearance of the parasites and desquamation.

It was quickly learned that the technic is not applicable to "mass production." In one instance, an attempt was



ade to examine 80 specimens collected within the space of approximately 30 minutes during a draft board examination of Negro males. It was found that the pressure of doing so many searches led to an unavoidable tendency to dismiss apparently negative specimens without adequate care. It was also found that after the first few specimens had been examined, motility in the remainder was reduced. It was also noted that if the patient had recently emptied his bladder and could void only a few cubic centimeters of urine, identification frequently was impossible, because time had not been allowed for the regeneration of the protozoa.

#### **PATHOGENICITY**

When one is faced with the fact that nearly 28 percent of Negro males harbor the parasite, the question arises whether the organism is pathogenic or should be regarded as a more or less "normal" inhabitant of the urogenital tract. Discussion of this in relation to female infestations has been extensive, but the matter apparently has not been settled to general satisfaction. Infestation without symptoms has led many workers to conclude that the organism is saprophytic. Others believe that to cause symptoms it must be symbiotic with a streptococcus or other organism. A few have thought that *T. vaginalis* is quite capable of causing lesions in its own right. The present studies suggest that, in the male, trichomoniasis is not associated with any constant bacterial flora, and there is even some evidence that it may thrive in prostates in which the secretion is bacteriologically sterile by all techniques as yet employed. It has been true that whereas the individual infested may have no spontaneous complaints referable to the genito-urinary tract, in almost every instance careful history taking will elicit some distinct variation from normal which perhaps can be ascribed to the presence of the flagellates. Histopathologic studies of prostatic tissue removed by transurethral prostatic resection, by perineal prostatectomy, and at autopsy are under consideration at present and may offer valuable clues on the subject. For the pur-

poses of this preliminary report it is impossible to say that the organism is a pathogen, but its association with purulent discharges, strictures, and with chronic prostatitis in so many instances places it under more than a little suspicion.

#### **SYMPTOMATOLOGY**

In the 44 cases analyzed, nocturia was the foremost symptom. Forty-eight percent of the patients complained of nocturia which was out of keeping with what might be regarded as "normal" for the age of the patient. Burning on urination was present in 13 percent, frequency during the day 11 percent, and itching in 11 percent. A discharge or morning drop was present in 48 percent but was frequently not regarded as a complaint.

In 61 percent of the cases, the patients gave a definite history of urethral discharge at some time in the past. Of these, 13 percent could be positively identified in the hospital records as being gonococcic in origin. Thirty-two percent either gave a distinct history of antisyphilitic therapy or were found, in the course of hospital studies, to be syphilitic. Eighteen percent were known to have or were found to have urethral strictures. Only 3 patients in the 44 could be said to have a completely asymptomatic infestation, although in many cases it was impossible to be sure that the symptoms were due to the presence of the trichomonads.

#### **THERAPY**

Those workers who believe that *T. vaginalis* is purely saprophytic hold that it requires little or no treatment. Some insist that it is an accidental inhabitant of the urethra, is self-limited, and will disappear if left alone. Such has not been the experience in this series. Three patients are known to have been infested for 5 years or more without intervening sexual exposure to cause reinfestation, if what appear to be reliable stories may be believed. A number of cases have been observed in which the infestation was constant through 2 or more months of hospitalization. Liston and Lees have advocated therapeutic creation of a pH in the urine unfavorable to the growth

of *T. vaginalis*. Many of our cases were carried to the safe extreme of acidity and maintained there (pH 4.5); after a week or two they were switched to alkalinity and maintained at a pH of about 8.5 without effectively eliminating the parasite. Acidification has seemed to be somewhat more inhibitory to growth of the organisms than has alkalization.

Numerous authors have advocated some form of heat. When it is realized that the thermal death point of the organism lies around 48° or 49° C. it can readily be appreciated that heat cannot be relied upon as an effective agent. Forty-two degrees centigrade is a fair rectal temperature to achieve with any ordinary apparatus without running the risk of damage, and this temperature has been reached in many of the cases under study. The organism has appeared to thrive over a period of 8 to 14 days with daily treatments with long-wave diathermy.

Virtually every applicable solution for urethral irrigation has been tried; notably protargol, potassium permanganate, silver nitrate, mercurochrome, silver picrate, acriflavine, metaphen, oxycyanide of mercury, and hydrogen peroxide. To these can be added zephiran, which has been used in a portion of the present cases. Comparative studies of many of these solutions have been made in vitro, but for all practical purposes almost any one of them will kill the organisms in the urethra if left for a sufficient time. The difficulty lies in the fact that none of them will reach the organisms in the prostate, from whence the urethra is continually reinoculated. Individual cases have been treated with every one of the mentioned solutions, but currently we are using either zephiran 1:3,000 or silver picrate 0.5 percent or in 0.25 percent water-soluble jelly. None of the prostatic infestations appear to have been benefited by this therapy alone.

In only 2 cases with proved infestation of both the urethra and prostate have we apparently succeeded in eliminating the parasites. In each case this was accomplished by an intensive inpatient regime consisting of daily diathermy to the prostate, prostatic massage every other day,

strong alkalization of the urine for a week, followed by strong acidification for a week or longer, and the use throughout the treatment of urethral irrigations with zephiran or silver picrate. It must be added, however, that 2 other patients similarly treated either continued to show parasites or promptly resumed showing them on cessation of therapy. In each instance the patient showed no evidence of stricture or other genital urinary disease except chronic prostatitis.

We have hoped to discover some successful therapy for this infestation, but candidly, none have been found up to the time of this report.

Selection of therapy depends to some extent on the distribution of the infestation. Three cases were found in which infestation was limited to the preputial sac in uncircumcised individuals; no therapy beyond instruction in cleanliness was necessary. In the remaining 4 cases, only one persistently showed urethral infestation without ever showing the organisms in the prostatic secretion. In those cases associated with stricture it appears of paramount importance to dilate the stricture adequately. In all outpatient cases it seems essential either to interdict intercourse, or to insist on protected intercourse to prevent reinfestation. Because of the uncontrollable nature of this factor, we have chosen to concentrate our experiments with therapy on patients who are in the hospital and are known not to be having intercourse.

The name "*Trichomonas vaginalis*" has long been used in the literature of gynecology and parasitology. To attempt to replace it may be difficult indeed, but there is distinct merit in such a move. A parasite which infests as high as 27.4 percent of certain portions of the male population does not deserve a name which restricts it to the female sex. "*Trichomonas genitalis*" would be more truly descriptive of the habitat of the organism and at the same time would assist in impressing on the profession that infestations of males as well as females are to be considered.

I wish to acknowledge the assistance and advice of Dr. Marion M. Brook, Dr. Hugh H. Young, and Mrs. Mary E. Turner.

*Venereal Disease Information, June 1944*



# Technic of Follow-Up of Selective Service Registrants With Syphilis in Philadelphia<sup>1</sup>

Alice M. Kresge, R. N.<sup>2</sup>

Shortly after the inception of the Selective Service Act in November 1940 the Institute for the Control of Syphilis, Hospital of the University of Pennsylvania, assumed responsibility for the immediate pervision of the follow-up of those registrants in Philadelphia who had positive or doubtful serologic tests for syphilis. All registrants called up for examination had received serologic tests. The Kline test was used routinely on all blood specimens, and all doubtful specimens were retested with the Kolmer technique. Data obtained on the prevalence of syphilis among selectees showed the Pennsylvania problem to be that of an average industrial State, but the Philadelphia rate of 41.7 per thousand proved the highest of any city with over a million population. Subsequent analyses have shown this to be due, at least in part, to the fact that Negroes make up 2.9 percent of the total population of the city.

There are 85 local boards in Philadelphia. These boards reported to State Selective Service Headquarters, which in turn reported to the State Department of Health, the names of all registrants who had positive or doubtful blood tests. In the larger cities, the State Department of Health turned over the investigation of seropositive cases to local health departments. This procedure required from 3 to 6 weeks on an average from the time of the blood test until follow-up was instituted. The Division of Venereal Disease Control of the Philadelphia De-

partment of Public Health was then in the process of organization and lacked the personnel to assume complete responsibility for follow-up of registrants. A cooperative project with the Institute for the Control of Syphilis was organized by the health department.

When the names of registrants for follow-up were received by the institute from the health department, the following procedure was used: A form letter was sent to the registrant, informing him that the blood test taken when he was examined for Selective Service showed that he might need treatment. Syphilis was not mentioned. The letter advised him to report to a private physician or a clinic of his choice, and gave the address and hours of a clinic near his home. He was requested to give the letter to the physician. This letter provided space for the physician to indicate that the registrant had reported, and the date treatment was started; or if treatment was not begun, why. If the registrant was already under treatment, the physician was asked to furnish the date treatment had been begun. A stamped, addressed envelope was enclosed to facilitate the return of these forms.

Of 4,661 letters advising medical care, 1,916 (41.1 percent) were returned satisfactorily completed. In many of these satisfactory cases, the registrant visited the institute worker. Some wished assistance in making plans for treatment, others who had already received treatment questioned the necessity for further medical supervision; still others desired more information about the test.

If nothing was heard from the registrant or his physician within 2 weeks, a second and somewhat authoritative letter was sent. An estimated 17.4 percent of the total number responded satisfactorily to this second letter.

<sup>1</sup> Description of epidemiologic program in Philadelphia as carried out jointly over a 2-year period by the Philadelphia Department of Public Health, Division of Venereal Disease Control, and the Institute for the Control of Syphilis, Hospital of the University of Pennsylvania.

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If no response was obtained within another 2 weeks, the registrant was visited at his home. Although comparatively few of the men could be found there during the day, every effort was made to interview them in their homes. This gave the public health nurse valuable opportunity to use her experience as a health teacher, in interpreting the results of the blood test and explaining the need for medical supervision. Some lay investigators, who had been given special training at the institute and who worked under public health nursing supervision, were used to good advantage for this work.

If the registrant was not at home, a note in a plain sealed envelope was left for him. The tone of this note was somewhat peremptory and asked the registrant to notify the institute worker at once regarding his plans for medical care, in order that his local board could be notified. This note brought replies largely from those men who feared the authority vested in the local board. In view of the necessity for sustained treatment, the lasting value of this approach may be questioned.

In some instances, a second home visit was made. The desirability of this visit was determined by several factors, including the registrant's age, his home situation, and his previously expressed interest. If this effort was unsuccessful, the record was closed by the institute as an unsatisfactory disposition.

In all instances, at the completion of the follow-up by the institute, the form was returned to the health department, which then notified the local boards of those registrants who had made no response to follow-up efforts. Satisfactorily completed forms were sent to the State Department of Health.

During the 2 years from July 1, 1941, to June 30, 1943, a total of 4,861 cases were investigated. Of this number, 3,504 (72 percent) were satisfactorily closed as to follow-up. As a direct result of the follow-up work, 48 percent of the total number investigated were placed

under treatment, and 16.3 percent were found to be already under treatment. The time of beginning treatment was unknown in 7.6 percent of the cases.

Table 1 summarizes the satisfactory dispositions.

TABLE 1

	Private physician	Clinic	Total	Percent of 4,861 investigated
Under treatment as result of follow-up.....	784	1,557	2,341	48.2
Already under treatment.....	331	463	794	16.3
Time of beginning treatment unknown.....	84	285	369	7.6
Total.....	1,199	2,305	3,504	72.1

Service for a group comprising 8.5 percent was continued after July 1, 1943, by the Division of Venereal Disease Control, Philadelphia Department of Public Health.

When the program for the follow-up of deferred Selective Service registrants with positive serologic reactions was initiated, Philadelphia had no means for checking registrants with positive tests against the registry of patients known to be under treatment. The Central Registry now in operation will eliminate the need for following up most of those patients already under treatment.

Table 2 summarizes the results of the 4,861 investigations on registrants with positive or doubtful serologic reactions in Philadelphia from July 1, 1941, to June 30, 1943.

TABLE 2

	Number	Percent
Registrants known to be under treatment.....	3,504	72.1
Unresponsive to follow-up efforts.....	420	8.6
No longer in Philadelphia but whereabouts ascertained.....	74	1.5
Not located.....	300	6.2
Inducted into military service.....	59	1.2
Incarcerated in penal institutions.....	23	0.5
Subsequent serologic tests negative.....	25	0.5
Deceased.....	10	0.2
Miscellaneous.....	34	0.8
Disposition pending.....	410	8.4
Total.....	4,861	100.0

The efforts made to locate the men and to place them under medical care are shown in Table 3.

TABLE 3

Initial letters advising medical care-----	4,661
Second letters-----	2,745
Letters to verify information regarding treatment-----	575
Personal letters in reply to registrants' inquiries-----	337
Home visits-----	2,448
Telephone calls initiated by staff, to physicians, local boards, etc.-	599

During the 2 years the number of office and telephone interviews were not tabulated. However, in the 4 months from March 1, 1943, to July 1, 1943, a total of 193 telephone contacts were received from registrants who wished further assistance.

An attempt has been made to estimate the cost involved in placing one registrant under treatment. The approximate expense in salaries of clerical assistants, public health nurses and lay follow-up workers, carfare, stationery, postage and telephone, amounted to \$7,449.36 for the 2 years, giving an average cost of \$3.18 for placing one registrant under treatment. This figure is the cost only for those patients known definitely to have begun treatment as a result of follow-up efforts and does not include the 7.6 percent for whom the time of beginning treatment was unknown or the 16.3 percent found to be already under treatment. If these are included, all of which are considered satisfactory dispositions, the total cost per patient was \$2.13.

In an early study made in this clinic by Pugh, Stokes, Brown and Carnell, successful follow-up visiting was estimated to cost \$5.99 per patient. This figure cannot be compared with the cost of \$3.18 in placing a registrant under treatment, as the situation involved in restoring a lapsed patient to treatment differs from that of placing an individual under medical supervision and closing his record when he has had one treatment. A study

by Louise B. Ingraham in this clinic showed the cost of arranging one contact examination to be \$5.22. The cost of instituting treatment for one registrant would obviously be less since almost 60 percent of the follow-ups required correspondence only. When home visits were made, it was usually impossible to interview the registrant personally; messages were left, and consequently a large number of visits could be made.

The follow-up program undertaken cooperatively by the Division of Venereal Disease Control and the Institute for the Control of Syphilis was carried out from a teaching center, basing all case-finding and case-holding efforts on definite principles. There was no departure from these principles in the follow-up of registrants.

Since it is believed that the element of fear is more likely to hamper than to aid a control program and that it rarely keeps a patient under treatment for any length of time, the basis for the approach to the registrant was protection of his health. He was advised to see his doctor for this positive reason. That he was forced to comply with Selective Service regulations in submitting to a blood test, in itself, constituted a show of authority. Any further authoritative approach seemed unsound in view of what was hoped would be accomplished through contacting each registrant, i. e., educating him to the significance of a blood test and placing him under regular treatment if a diagnosis of syphilis was established.

A fair, considerate procedure with individuals and an appreciation of their problems are basic to any sound program. Innumerable personal and telephone interviews with registrants took place. Some registrants were puzzled, apprehensive, or shocked. A large majority wanted to do something about the fact that they had positive serologic tests. Many wanted to know more about the meaning of the test. Many had financial problems, or problems where hours of employment made reporting for treatment difficult. During the 2-year period of the institute's supervision of the pro-



gram, 337 personal letters were written, each considering an individual problem presented by the registrant. If an interview was desired, it was held at the Institute for the Control of Syphilis in the University Hospital with the public health nurse who was on the institute's staff.

Every effort was made to give the registrant responsibility and a chance to make his own decisions. He was asked to choose his own physician or clinic and to notify the institute worker regarding it. Based on the principle that individuals do best when given an opportunity for self-direction, the initial letter to the registrant suggested a course of action, but did not command that medical care be sought. Thinking was in terms not only of placing the registrant under medical care, but, insofar as possible, instilling an attitude which would aid in holding him to treatment after he did report to a physician. It cannot be reiterated too often that the way the patient feels about having syphilis is one of the most important factors in syphilis control. An authoritative approach has real value when other methods fail, but experience has shown that it seldom holds the patient to regular, continuous treatment over a long period, nor is an authoritative approach likely to make the patient an educational agent for a syphilis control program.

Figures are not yet available as to the amount of follow-up effort required to hold the registrant to treatment. It is felt that these patients probably require considerable effort. Although the authoritative approach was not used until other measures had proved ineffective, most registrants were aware that Selective Service regulations are backed by authority. It would be difficult to estimate how potent a factor this is in obtaining either the satisfactory or the unsatisfactory dispositions. Local boards varied greatly in the amount of responsibility which they felt should be assumed, and they had no coordinated plan of action. Even though they were not responsible for the follow-up, they occasionally

brought pressure to bear on the registrant.

*Summary.*—A procedure is described which was used in Philadelphia for the follow-up of registrants examined for Selective Service who were found to have positive or doubtful serologic tests. The total cost of follow-up efforts for each registrant known to be under treatment for syphilis when his record was closed by the Institute for the Control of Syphilis, was \$2.13. Satisfactory disposition was obtained in 72.1 percent of the cases followed for 2 years. The follow-up was based on a positive approach to the registrant, which utilized the registrant's interest in himself and his desire to maintain his good health.

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## DIAGNOSIS

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**The uses and limitations of the serum tests for syphilis.** L. W. Harrison and T. E. Osmond. *Brit. J. Ven. Dis.*, London, 19: 108-118, Sept. 1943. *Abst. in Bull. War Med.*, London, 4: 350-351, Feb. 1944.

The authors discuss the causes, prevention and detection of false positive reactions, and the prevention of a false



agnosis of syphilis in cases where no clinical evidence is present. These errors in diagnosis may be due to faulty methods or faulty technic.

According to the literature, conditions which may give a false positive reaction for syphilis are yaws, leprosy, trypanosomiasis, relapsing fever, malaria, scarlet fever, tropical ulcer, pellagra, beriberi, pneumonia, late tuberculosis, diabetes mellitus, enteric fever, scleroderma, malignant disease, and vaccination.

The authors suggest the following procedure when a positive reaction for syphilis is not supported by any clinical evidence: (1) Exclusion of laboratory error by submission of another specimen, which should also be tested in at least one other laboratory. (2) In the event of the positive reaction being repeated, application of a Richardson complement fixation and a Kahn verification test. (3) Careful inquiry respecting any recent illness due to any of the conditions already mentioned as being liable to cause false positive reactions. (4) Further clinical examination, including radiography of the cardiovascular system and tests of the spinal fluid. (5) Examination of siblings.

In cases where examinations show nothing definite, the authors advise withholding treatment while further tests are made.

**Study of 1,000 cases of genital chancre: Diagnostic value of darkfield examination.** (Estudio de 1,000 casos de chancros genitales. Valor diagnóstico de la investigación ultramicro scópica.) Carlos Julio Alarcón and Tomás Genatios. *Rev. san. y as. soc.*, Caracas, 8: 989-999, Oct. 1943.

The authors studied 1,000 cases of genital chancre, 943 (94.3 percent) in men and 57 (5.7 percent) in women, the women usually being in the secondary stage before they sought medical advice. They varied in age from 10 to 60 years, the large majority of cases falling, however, into the 10- to 20- and 20- to 30-year age groups. For both men and women com-

bined, 36 percent of chancres occurred in the 10- to 20-year and 53 percent in the 20- to 30-year age groups; for men alone 34.8 percent occurred in the 10- to 20-year and 53.9 percent in the 20- to 30-year age groups; for women alone 56.1 percent occurred in the 10- to 20-year and 40.4 percent in the 20- to 30-year age groups. One child 5½ years of age was seen who had contracted a chancre from a homosexual. In the 10- to 20-year age group the majority were 15 years old. Single lesions were observed in 700 (70 percent) and multiple chancres in 300 (30 percent). The darkfield examination was positive in 256 cases (25.6 percent). In 56 cases the Ducrey bacillus was also present. Among a total of 572 cases examined for the Ducrey bacillus, 260 (45.45 percent) were positive.

In studying the relationship between the darkfield findings and the Kahn reaction the authors divided the patients into two groups, first those whose reactions prior to the development of chancre had been positive and second those in whom the reactions were positive following the development of the chancre. In the first group there were 200 persons, of whom 50 had had positive reactions; in the second group 680 persons, of whom 306 had had positive reactions.

Among a total of 2,859 chancres diagnosed in 5 venereal disease clinics in Caracas 275 were seronegative, 568 seropositive, and 2,016 were soft chancre or chancroid. The darkfield examination was positive in 516 cases.

**Hippuric acid liver-function test during treatment with arsenicals.** R. W. Riddell and T. E. Anderson. *Lancet*, London, 1: 275-276, Feb. 26, 1944.

A series of hippuric acid tests were carried out on patients with syphilis undergoing arsenotherapy in a military hospital.

Quick's (1933) clinical method was adopted. It consists of administration, orally, of 6 gm. sodium benzoate, collecting the total urine excreted during the following 4 hours, and estimating its hippuric acid content. This method is

inexpensive and requires a minimum of technical training and apparatus.

In all, 708 tests were carried out upon three groups, the first being 50 normal males chosen as controls; the second, 157 cases of untreated early syphilis investigated as they arrived at the hospital; the third, 188 cases of early syphilis already under arsenical treatment.

The results indicated that the hippuric acid test revealed impairment of liver function in a significant proportion of patients receiving arsenical treatment for syphilis, but the impairment bore no relation to the total quantity of drug given, and was attributable to individual sensitiveness to arsenicals.

The failure of detoxifying function detected by this test preceded the onset of jaundice and the appearance of bile products in the urine. The warning thus given made it possible to stop arsenical injections and avoid additional toxic effects. Nevertheless, jaundice ensued in about 30 percent of the cases in which arsenical treatment had been stopped.

Tests made every 2 weeks in cases of postarsenical jaundice showed a steady and sometimes rapid return to normal function. A low hippuric acid test result does not necessarily imply a fatal outcome or irreparable damage to the hepatic detoxifying mechanism.

Institution of routine hippuric acid tests during treatment with arsenicals is recommended wherever practicable.

**Primary and secondary syphilis; chronic lymphatic leukemia.** A. Benson Cannon. (Tr. New York Dermat. Soc.) Arch. Dermat. & Syph., Chicago, 49: 145, Feb. 1944.

A case of a 34-year-old man is presented. On admission to the hospital he had a penile lesion and a generalized eruption, a sore throat and enlarged lymph nodes, of 3 weeks' duration. The penile lesion contained spirochetes and precipitation reactions were positive.

Examination disclosed a generalized, grouped, papular eruption on the trunk, face and extremities, including the palms and soles. Some of the lesions were

scaly. On the glans penis there was a sloughing lesion; the superficial lymph nodes were enlarged, and there were papules on the left breast, in the right supraclavicular region and in front of one elbow. The right tonsil and surrounding tissues were swollen and dark red, with a sloughing ulcer. The blood serologic reactions were positive and darkfield examination revealed spirochetes.

Daily injections of arsphenamine were given; after 1.7 gm. all lesions disappeared except for those on the left breast, in the right supraclavicular region and on the elbow, and the ulcer of the tonsil. Because of the persistence of the enlarged nodes and their unusual size, the persistence of the few lesions, and the ulcer on the tonsil, lymphoblastoma was suspected. A blood count revealed 60,000 leukocytes, 78 percent lymphocytes and 11 percent young lymphoblasts, which confirmed the diagnosis of lymphoblastoma.

In the discussion, it is pointed out that a patient may present himself for some other cutaneous condition and during the routine examination of the blood the leukemia is discovered, which happened in the case reported.

**Infectious and serologic relapse during intensive arsenotherapy of early syphilis.** Arthur G. Schoch and Lee J. Alexander. Am. J. Syph., Gonorr. & Ven. Dis., St. Louis, 28: 221-227, Mar. 1944.

Intensive arsenotherapy of early syphilis, providing it is a method in which mapharsen alone is used, results in failures in about 20 percent of the cases. The treatment failures may be classified as relapse, progression of the disease, or treatment resistance. They usually occur during the 6 months' period immediately following completion of treatment.

During the past 15 months the authors have treated over 600 patients with early syphilis at the Dallas Syphilis and Venereal Clinic, Parkland Hospital. The method of treatment was that recommended by Eagle and Hogan, consisting of 3 injections of mapharsen per week for



weeks. They report 4 cases in which treatment failure occurred during the course of treatment, which they regard as an unusual occurrence. In all of the patients there was a response to the drug at the beginning of treatment (clinically in all, serologically in 2), but before completion there was definite and undisputed evidence of relapse. One patient, during the second month of treatment, developed a florid, large papular secondary syphilid involving the hands and forearms; a second and a third patient progressed serologically from negative to positive, and a fourth had a serologic relapse during the second month of the second course of treatment. These cases are reported in detail.

The authors think it is possible that the factors responsible for failure during treatment may be identical with factors which result in failure following intensive therapy.

#### **Syphilitic fever in present-day syphilis.**

Leon Goldman, Norbert P. Ringelman and Harry L. Claassen. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, 28: 200-217, Mar. 1944.

A study of the incidence and intensity of true syphilitic fever in present-day syphilis was made on 2,519 unselected hospital patients with all types of syphilis at the Cincinnati General Hospital from 1937 through 1942.

Of 33 cases of primary syphilis, 3 had fever which could have been due to syphilis. Of this group, 23 were afebrile and 7 had fever associated with chancroidal infection. Among 129 cases of secondary syphilis, there were 14 (11 percent) with true syphilitic fever, 103 afebrile, and 12 cases with fever due to other causes. True syphilitic fever in early syphilis responded rapidly to arsenotherapy.

In 1,819 cases of latent syphilis, only 1 (0.05 percent) was diagnosed as a true syphilitic fever. This was a case of a 37-year-old white woman first seen in 1936, complaining of headache and fever with a history of sinusitis. Examination

showed her blood serologic tests positive, spinal fluid negative, white blood count varied between 7,600 and 6,000, normal differential count. Chills and elevation of temperature followed 0.3 gm. neoarsphenamine. She then received bismuth and 6 days later 0.4 gm. neoarsphenamine without reaction. The temperature rapidly dropped to and remained at normal. Fever of latent syphilis was suspected. She was discharged from the hospital and continued antisyphilitic treatment at intervals until 1942, when the spinal fluid test was reported positive (it had been negative and the blood serologic test positive the previous year). The history of sinusitis was confusing in this case, but the authors believe that the persistence of the fever, response to therapeutic tests and the failure of the fever to recur under irregular antisyphilitic therapy suggested that this may have been syphilitic fever. The patient developed neurosyphilis some years later.

Of the 464 cases of late syphilis, there were 353 afebrile, 30 febrile cardiovascular syphilis, 74 febrile neurosyphilis, and 7 miscellaneous types of febrile late syphilis. The incidence of true syphilitic fever in these cases was low. In most of the cardiovascular patients with fever this was due to "fever of congestive failure" or to local pressure phenomena plus infection. Except for a few instances, the fever of neurosyphilis was due to nonsyphilitic complications. Two of 13 cases of hepatic syphilis had fever due to this cause.

The series of congenital syphilis was too small and data on these cases too meager to permit of a critical analysis.

Syphilitic fever in these cases was usually low grade in intensity and had no special type of curve configuration. The authors believe that the lower incidence and the relatively insignificant role of fever in the symptomatology of syphilis of today over its apparent important role in syphilis of past years is additional clinical proof of the changing character of syphilis.

## **The clavicular sign in congenital syphilis.**

K. D. Lahiri. *Indian M. Gaz.*, Calcutta, 78: 431-432, Sept. 1943.

The enlargement of the sternal end of the clavicle in congenital syphilis in children approaching puberty is an important diagnostic sign of congenital syphilis.

The author reports 5 cases, ranging in age from 8 to 12 years. The blood Wassermann reaction was positive in all cases. Other indications of congenital syphilis in these patients were osteomyelitis of the femur and chronic rhinitis in 1, keratitis in 3, and osteomyelitis of the tibia and chronic arthritis in 1. Four of the cases were unilateral and 1 bilateral. Following antisyphilitic treatment, the swelling partially subsided in 2 cases, and almost disappeared in 1. In 2 of these cases there was no marked change following antisyphilitic treatment.

Other similar cases are reported in the literature. Nair and Chetty, in 1942, reported 130 cases of congenital syphilis, and of these 103 showed the clavicular sign. They found that the inner third of the clavicle was visibly thick and enlarged, and that the enlargement was unilateral, being on the right side in right-handed persons and on the left side in the left-handed.

## **Brief notes on recent investigations carried out in the pintagenic areas of Venezuela in relation to the actual state of knowledge of carate or pinta.**

(Breves notas sobre ultimas investigaciones verificadas en las zonas pintogenas de Venezuela en relación al estado actual del conocimiento del carate o mal del pinto.) A. L. Briceño Rossi and David R. Iriarte. *Rev. san. y as. soc.*, Caracas, 8: 1001-1013, Oct. 1943.

The authors have tried various methods and media in painstaking attempts to culture the treponeme obtained from lesions of carate or pinta and to reproduce the lesions in animals (guinea pigs, rabbits, cats, dogs)—all without success. In the pintagenic zones of Venezuela, domes-

tic animals such as cattle, horses, pigs, goats, rodents, and monkeys were found to be free of the lesions of pinta and it was impossible to produce these lesions experimentally in them. The authors concluded that pinta is a disease of human beings, like leprosy.

In Estados Miranda and Barinas erythemato-squamous, lichenoid, and psoriasisiform lesions were particularly common. Dyschromic lesions were found more frequently in children than in adults. Early lesions are rarely observed because of the indifference of the people to the disease, which prevents them from seeking medical advice; the lesions apparently develop over a period varying from 6 months to 10 or more years.

The authors point out that the initial lesions of pinta may be erythemato-squamous, lichenoid or papular and that they correspond to the pintides of León y Blanco. Darkfield examination of fluid obtained from the scarified lesion is necessary to establish the diagnosis. If treponemes are found, antisyphilitic treatment is indicated; if they are absent, non-specific ointments such as salicylic acid ointment should be used. In case treatment with ointment fails to cure the lesions, bismuth injections should be given since the lesions may be early pinta.

The Wassermann, Kahn standard, Kline, Chediak, and Briceño Rossi serologic tests for syphilis were applied to patients with pinta. In active, darkfield-positive pinta (definite dyschromic spots) positive serologic reactions were obtained in 100 percent of the cases and the verification test gave the specific type of reaction. In treated or old cases in which only vitiligoid lesions remain, the serologic reactions were found to be positive in from 52 to 81 percent of cases.

Of 10 patients with treponeme-positive erythemato-squamous lesions 60 percent had positive reactions to the Briceño Rossi and the verification tests.

The examination of triturated insects with the darkfield failed to reveal Treponema. Although the entomologic studies and their relationship to the possible transmission of pinta are being continued,



e authors believe that prolonged congestion, similar to that observed in leprosy, plays the major role in the transmission of the disease.

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## TREATMENT

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**Penicillin in treatment of gonorrheal conjunctivitis: Report of a case.** Walter P. Griffey. Arch. Path., Chicago, 31: 162, Feb. 1944.

A 24-year-old man was first admitted to the U. S. Marine Hospital at Brighton, Mass., on May 24 with the diagnoses of gonorrheal urethritis and gonorrheal conjunctivitis. The urethral discharge appeared 6 days, and inflammation of the right eye 2 days previous to admission. Sulfathiazole therapy was instituted and sulfathiazole ointment, boric acid and cold compresses were applied locally. Bacterial vaccine made from the typhoid bacillus U. S. P. was given intravenously. The oral use of sulfathiazole was continued until July 2, at which time the urethral discharge had subsided considerably but the ocular infection, with a copious purulent discharge, persisted.

The patient was admitted to the U. S. Marine Hospital, Staten Island, N. Y., on July 3, 1943. Examination of the infected eye showed gram-negative intracellular diplococci, which were identified as gonococci by cultural studies, and gonococci were discovered in the urine. Therapy consisted of intramuscular injections of 25,000 units of penicillin sodium every 3 hours for a total of 10 injections. Hourly examinations of spreads and cultures of the conjunctival secretions showed them to be positive for *Neisseria gonorrhoeae* for 5 hours, after which time they were persistently negative. Cultures of the sediment of the specimens of urine were positive 3 hours after treatment, but after 5½ hours were negative. Prostatic secretions gave negative results. Approximately 10 hours after the beginning of penicillin therapy the exudate of the eye had greatly diminished, and after the in-

flammation subsided the eye returned to normal.

**"Drug fever" accompanying second courses of sulfathiazole, sulfadiazine and sulfapyridine.** Harry F. Dowling and Mark H. Lepper. Am. J. M. Sc., Philadelphia, 207: 349-353, Mar. 1944.

The authors have analyzed the data on all the patients coming under their observation who have received more than one course of the sulfonamide drugs and who did not develop fever during the first course.

Among 144 patients who received a second course of sulfathiazole, sulfadiazine or sulfapyridine after a varying interval of time had intervened since the first course of the same sulfonamide, 16 (11.1 percent) developed drug fever. Eleven of these patients developed concomitant dermatitis, which in 2 instances was associated with conjunctivitis.

Among 169 patients who received a second course of sulfathiazole, sulfadiazine or sulfapyridine following a first course of another sulfonamide, 6 (3.6 percent) developed drug fever.

Among 737 patients who were observed during a single course of therapy with sulfathiazole, sulfadiazine or sulfapyridine, 37 (5 percent) developed febrile reactions.

Febrile reactions were more frequent following a second course of sulfathiazole, as well as during a single course of sulfathiazole, than was the case with sulfadiazine or sulfapyridine.

Three to 6 courses of the same sulfonamide were given to 12 patients, none of whom developed febrile reactions.

It is concluded that, when a second course of a sulfonamide must be given to a patient, regardless of the interval following the first course, another sulfonamide drug should be given.

**Renal complications following sulfonamide therapy.** Temple Ainsworth. Mississippi Doctor, Booneville, 21: 239-243, Feb. 1944.

Six cases of severe renal damage following sulfathiazole or sulfadiazine

therapy are reported. Three of the cases terminated fatally. The patients had been given sulfonamides because of chronic prostatitis and fibrositis (1 case), pus cells in the urine following a transurethral prostatectomy (1 case), sore throat (2 cases), cellulitis of right leg (1 case), and fever following a right nephrectomy (1 case). The author feels that these conditions were not sufficiently serious to warrant the administration of sulfonamides.

Some of the factors which help to prevent renal complications are to administer the smallest amount of the drug that will accomplish the desired result; keep the urinary output at least 2,000 cc. daily; give sufficient alkali to keep urine above 7.2 pH; examine urine at frequent intervals for blood or crystals; give drug cautiously and discontinue it on appearance of blood in urine, decrease in urinary output or drug fever.

Some suggested methods of treatment for renal complications are given.

In the discussion, Shands stated that he had reserved the use of the sulfonamides for gonorrhea, blood poisoning, pneumonia and peritonitis.

The author stated that he has 2 additional patients (one an 18-year-old boy) in the hospital who are dying as a result of sulfonamide therapy.

**Sulfonamide-resistant gonorrhea in the male: A preliminary report on a proposed method of therapy.** Alfred Cohn and Borris A. Kornblith. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, 28: 179-186, Mar. 1944.

This is a preliminary report of the results obtained with combined vaccination and chemotherapy in 22 unselected male cases with gonococcic infections resistant to sulfonamides. There were 3 cases with anterior and 5 with anteroposterior urethritis, and 14 with urethritis complicated by prostatitis. All cases had failed to respond to at least two, and some to three courses of sulfonamide therapy.

Gonococcus vaccine for 10 consecutive doses in increasing amounts, following

an initial injection 0.01 cc., was given, preferably on alternate days, reaching a total dosage of approximately 0.62 cc. Sulfathiazole administration was begun with the fifth injection and was continued in conjunction with vaccination. A total of 28 gm. sulfathiazole was given in doses of 4 gm. daily, over a period of 7 days.

The 8 cases of anterior and posterior urethritis were all cured by combined vaccine-sulfathiazole therapy. Of the 14 cases of urethritis complicated by prostatitis, 4 responded promptly to one course of this combined therapy, 4 relapsed within 1 week of apparent cure, 1 was cured after repeated prostatic massages and a third course of the therapy, and 5 cases remained resistant to repeated courses of this and other forms of therapy and are still under investigation. Of the 4 cases which showed recurrences, 3 responded to a second course of combined vaccine-sulfathiazole therapy and 1 became delinquent.

A contact case is cited, in which a male patient with an in vitro resistant strain infected his wife. Although the strain isolated from the wife was resistant in vitro, she responded promptly to one course (20 gm.) of sulfathiazole, while the husband was resistant to chemotherapy. These findings corroborated the importance of the host factor in determining the outcome of chemotherapy.

**Hyperthermia in the treatment of resistant gonococcal and non-specific urethritis.** A. J. King, D. I. Williams and C. S. Nicol. *Brit. J. Ven. Dis.*, London, 19: 141-154, Dec. 1943.

The authors report their results in 418 patients treated by hyperthermia. They classify these patients into three groups and report their findings in each group. Group A comprised 319 cases, of which 285 had uncomplicated urethral gonorrhea and 34 gonorrhea with local complication. In this group, following 8-hour fever sessions, 26 cases which had received no premedication showed immediate cure in 14; 28 cases receiving sulfonamide premedication, in 25; 195 cases receiving sulfathiazole premedication, in 180. Follow-



ing 6-hour fever sessions, 16 cases with sulfathiazole premedication and 1 with sulfadiazine gave immediate cure in 15. Following 3-hour fever sessions, 8 cases receiving no premedication gave immediate cure in 4. Forty-five cases received fever sessions varying in length from 4 to 7½ hours; of these, 9 cases receiving no premedication gave immediate cure in 2, and 36 cases receiving sulfonamide premedication in 26.

Group B comprised 23 cases which had been treated for gonorrhea but still had a persistent urethral discharge in which gonococci could not be found, or they had signs of infection in the urine. Of 20 cases receiving 8-hour fever sessions, 6 who had received no premedication gave immediate cure in 2 and 1 died; and in 14 who had received sulfathiazole medication, 11 were cured. In 3 cases given 6-hour sessions with no premedication, immediate cure was seen in 2.

Group C comprised 76 cases of non-specific urethritis. In 60 cases the 8-hour fever sessions were given; immediate cure was seen in 6 of 13 cases receiving no premedication, and in 30 of the 47 cases who had sulfonamide premedication. Six-hour fever sessions were given to 8 cases (7 having sulfathiazole premedication), with immediate cure in 4. Eight cases receiving less than 6-hour sessions gave cure in 2.

From the authors' findings, the length of the fever session seemed to make little difference when sulfonamide premedication was given. In resistant gonococcal urethritis, high fever with sulfonamide premedication is considerably superior to high fever alone. However, the authors feel that too few cases have been observed to draw definite conclusions as to the length of the fever session.

The authors used the Kettering hypertherm in all their cases. They stress the importance of skilled and experienced nursing care. Some of the complications encountered during their observations are given.

**Physiological and biochemical changes following hypertherm treatment.** John Wallace and S. R. M. Bushby. *Brit. J. Ven. Dis.*, London, 19: 155-166, Dec. 1943.

The authors investigated the physiologic and clinical changes occurring in patients undergoing hypertherm therapy for gonorrhea to ascertain whether additional sulfonamide chemotherapy increased the risks of such treatment, and to discover any prophylactic or therapeutic measures which would eliminate or minimize the dangers inherent in hypertherm therapy.

A total of 254 cases undergoing hypertherm treatment at 106° F. for 8 hours has been studied clinically by the authors. In 37 of these cases a detailed clinical, hematologic and biochemical investigation was made. The hematologic and biochemical observations in these cases were more or less the same in each instance, and the main points were: (1) There was a transient hemodilution and polymorphonuclear leukocytosis with a return toward the pretreatment levels within 24 hours; (2) there was a rise in serum bilirubin (clinical jaundice after 48 hours in 3 cases), and (3) there was a transient rise in nonprotein nitrogen, and a transient fall in the carbon dioxide content of plasma and in plasma chlorides, the blood sugar levels showing no significant change.

The most constant and prominent features were the development of anoxia and bilirubinemia, progressing to clinical jaundice in some cases. Hippuric acid tests showed a considerable reduction in liver function. Continuous oxygen and carbon dioxide therapy tended to lessen anoxia and to prevent the development of circulatory collapse. Vomiting has become less frequent since oxygen therapy is used. Circulatory collapse is a failure of the vasomotor and respiratory centers and is not due to a reduction in the circulating blood volume or to myocardial failure.

The length of treatment must be decided by the physician in each case, and the authors give some indications on which this decision may be based. Care-

ful prehypertherm and posthypertherm treatment should be given. Six grams sulfathiazole premedication does not increase the hazards of hypertherm treatment.

**The rapid treatment of syphilis.** James Marshall. *Nature*, London, 153: 187-189, Feb. 12, 1944.

An interesting account of the evolution of the arsenical treatment of syphilis is given, with special reference to intensive arsenotherapy.

The intensive treatment of syphilis offers in a short time as good, or even better immediate results than the standard treatment scheme, but with a greatly increased risk of toxic effects and of death four times as great. Thus the aim in research in the treatment of syphilis is to discover a scheme which will occupy the shortest possible time, which will be free of dangerous toxic effects, give a high percentage of permanent cures, and can be used on outpatients. A clue has been given in the animal research work of Eagle and Hogan, who found that the curative dose of mapharsen was largely independent of the time over which it was administered; if these considerations apply in human syphilis, a variety of possible schemes are suggested for trial.

The application of intensive treatment must be restricted. Its benefits are obvious among personnel of the Navy and Merchant Marine when it is remembered that many ships do not carry a physician, and that haphazard treatment on standard lines may be worse than no treatment at all. A potential use for intensive arsenotherapy may be among persons who have been reported through Regulation 33B and refuse to place themselves voluntarily under treatment. (The author states that such a policy is in operation in the United States.)

The author concludes that the treatment of early syphilis in the future may be a compromise between the present standard scheme and the intensive methods and will probably last from 4 to 10 weeks. The arsenical will almost cer-

tainly be an arsenoxide preparation injected by syringe at least 3 times a week, bismuth being used concurrently.

**Observations on the massive-dose arsenotherapy of early syphilis by the intravenous drip method.** IV. Three years of trial. Branch Craige, Jr., and Joseph F. Sadusk, Jr. *New England J. Med.*, Boston, 230: 314-318, Mar. 16, 1944.

The authors have used massive arsenotherapy for early syphilis for 3 years, during which time 80 treatment courses were given to 74 patients. None of their patients have experienced nitritoid crisis, nephritis, cerebral symptoms, hemorrhagic encephalitis or exfoliative dermatitis as the result of this treatment. They have had no fatalities. The Herxheimer reaction occurred in 27 cases, drug fever in 24, vomiting in 58, peripheral neuritis 3 weeks after treatment in 30, electrocardiographic changes in 56. The most serious toxic reaction seen in this series was motor neuritis and jaundice, which occurred in 1 case.

The authors made follow-up observations on their patients at monthly intervals for 6 months, and at 3-month or 6-month intervals thereafter. When possible, another lumbar puncture was performed after several months.

The cardinal points to be observed are establishment of the diagnosis of early syphilis; exclusion of patients with fever, liver disease or severe nephritis, and periodic follow-up visits with determination of whether retreatment is necessary on the basis of the serologic reaction 6 months later, or of relapse at an earlier date.

The advantages of this method of treatment are that every patient receives an amount of treatment that has been found sufficient for cure in four-fifths of the patients, that completion of a minimum adequate amount of treatment does not depend on the patient's return, and that when the patient leaves the hospital he is noninfectious.

In the authors' experience, satisfactory results were obtained in 79 percent of



the cases following massive arsenotherapy by the 5-day continuous intravenous drip method.

**Mapharsen in the antivenereal dispensaries of Caracas.** (El mafarside en los dispensarios antivenereos de Caracas.) Rafael Sánchez Pérez. *Rev. san. y as. soc.*, Caracas, 8: 979-988, Oct. 1943.

In 3 antivenereal disease clinics in Caracas (Central, El Quebrado, and San Juan) mapharsen has been extensively used during the past 3 years in the treatment of early syphilis, a total of 28,200 doses having been given. The period of observation following treatment has been too short to evaluate the effectiveness of this drug in preventing the complications of the disease, such as cerebrospinal and cardiovascular involvement.

In primary and secondary lesions treponemes were observed to disappear from the lesions in from a few hours to several days. The initial dose used was 0.04 gm. The spirocheticidal effect and the effect in reversing the blood serologic reactions compared favorably with that of neoarsphenamine.

Untoward reactions to mapharsen which were observed included digestive disturbances in 114 cases, fever in 15, pruritus in 3, mild dermatitis in 6, and icterus in 2. No serious or fatal reactions occurred.

**Studies on therapeutic procedures in latent and late syphilis. II. The quantitative serologic titers following intensive mapharsen drip therapy in latent syphilis.** Bernard I. Kaplan and I. Jay Brightman. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, 28: 192-199, Mar. 1944.

The authors give a summary of their studies on therapeutic methods applicable to the latent and late stages of syphilis which were begun at Sing Sing Prison in 1939.

This report includes the serologic studies made upon 156 patients, 23 with early latent syphilis and 133 with late latent syphilis. These cases were fol-

lowed for 6 to 36 months following mapharsen drip treatment, with or without adjunct fever therapy.

Among the 23 patients with early latent syphilis, 17 (74 percent) showed a fall in titer to 50 percent or less of the initial level following intensive intravenous drip therapy with mapharsen, 11 (48 percent) becoming seronegative. The course of the fall in titer in these cases is shown in a chart. Of the 133 patients with late latent syphilis, 41 (31 percent) showed a fall in titer to 50 percent of the pretreatment level, 4 becoming seronegative.

There was no essential difference in the results among those who did and those who did not receive adjunct fever therapy. The initial titer of the serologic test and the amount of mapharsen administered did not seem to influence the results.

**Malaria in neuro-syphilis 1923-43.** J. Ernest Nicole. *J. Ment. Sc.*, London, 89: 381-389, July-Oct. 1943.

The author reviews 604 cases of general paresis, taboparesis, tabes and meningovascular syphilis, which constituted 20 years' work.

Of the 604 cases, 424 were inoculated with malaria, but for various reasons only 401 actually had malaria. The intramuscular method was preferred. An attempt to induce a second attack was made in 100 cases, but in only 81 was this successful. A third attack was produced in 15 out of 27 attempts. No fourth attack was produced, though it was attempted in 5 cases. Good recoveries were seen even in acute and advanced cases. In some instances reinoculations resulted in improvements that would not otherwise occur.

Malaria alone gave fair results, but the addition of drugs, such as tryparsamide, led to an improved recovery rate. Other drugs which may be used are bismostab, bivitol, bisglucol, iodo-bismuthate of quinine, neosalvarsen, stovarsol, sodium stovarsol, and acetylarsen.

From charts on the serologic findings of these cases it is seen that a return to normality in the spinal fluid is to be

expected in a majority of cases provided sufficient time has elapsed following the malarial treatment, this condition being achieved much earlier in the case of the cell count and the protein content than in that of the globulin and the Wassermann tests, while the Kahn and the Lange tests are the last to cease giving the usual paretic readings.

**Recent advances in the treatment of syphilis.** Walsh McDermott. *M. Clin. North America*, Philadelphia, pp. 293-308, Mar. 1944.

The recent advances in the therapy of syphilis have been almost entirely in the field of the more rapid treatment of early syphilis. Large-scale experimentation with intensive arsenotherapy began with the 5-day drip therapy in 1938 and consequently it has been possible to study a number of these patients who have successfully passed a 5-year test. In October 1941, Eagle and Hogan began a large scale study of systems of triweekly injections of mapharsen over periods ranging from 6 to 12 weeks, some of which were supplemented by bismuth. A treatment system, including biweekly injections of mapharsen over two 10-week periods separated by 5 weekly injections of bismuth, has been adopted by the U. S. Army Medical Corps, the over-all duration of treatment being 6 months. Just what will prove to be the ideal total length of such treatments is hard to say, but some period between 6 weeks and 6 months will probably prove the most satisfactory.

Because of the small supply of penicillin available and the great demand for it for other diseases, it will probably be a long time before it will be used generally for early syphilis.

Dattner and Thomas are conducting a much shortened system for the treatment of neurosyphilis. This consists of induction of fever by malaria followed immediately by daily injections of 0.060 gm. mapharsen for a total period of 10 days only. Surgical treatment is being tried in primary optic atrophy.

The author has treated with safety in the past 6 years 100 patients with frank aortic syphilis by a modification of Moore's method.

**The experimental prophylaxis of chancroid disease—II.** Robert B. Greenblatt and Everett S. Sanderson. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, 28: 165-178, Mar. 1944.

Chancroidal lesions were induced in volunteers by the inoculation of scarified zones with various dilutions of a virulent strain of *Hemophilus ducreyi*. Small pustules appeared along the line of inoculation in 48 to 72 hours, which soon coalesced into a large pustule which usually ruptured within a few days, leaving a typical chancroidal ulceration with undermined edges and a dirty necrotic base. The lesions were from 1 to 1.5 cm. in diameter and healed within 7 to 14 days following sulfonamide therapy orally and/or locally.

The inhibitive effects on the growth of *H. ducreyi* in vitro were assayed for 8 arsenical compounds and 4 detergents. The arsenicals were A-10, 4289-SC, 12-A, 32, 38-b, 4-CONH<sub>2</sub>, 115-b and 140, and the detergents were ceepryn, igepon, phemerol and zephiran. The detergents, zephiran and phemerol, and the arsenicals, A-10, 115 and 32, were inhibitive at 1:10,000 dilution. Propylene glycol, used as solvent in these studies, showed no inhibition of growth of *H. ducreyi* in dilutions ranging from 1:500 to 1:10. The author's findings are given in a table.

Various medicaments were tested in the prophylaxis of experimental chancroidal disease: (1) Sulfonamides in water-miscible ointment bases: Sulfathiazole ointments proved more effective than sulfanilamide ointments, and the 20 percent concentrations of these sulfonamides proved slightly more effective than the 5 percent. A mixture of 20 percent sulfathiazole and 33 percent calomel in a water-miscible base proved more effective than 20 percent sulfathiazole alone. The former was effective in about 75 percent and the latter in from 40 to 65 percent.



(2) Arsenical compounds dissolved in propylene glycol: Six arsenical compounds dissolved in propylene glycol in dilutions varying from 1:1,000 to 1:100 proved to be ineffective prophylactic agents.

(3) Detergents in aqueous dilutions: Four detergents in 2 percent aqueous dilution were tested. Zephiran 2 percent aqueous proved to be the most effective prophylactic, being effective in 90 percent. Increased dilutions decreased its effectiveness. Phemerol and igepon were of little value and ceepryn entirely ineffective.

(4) The effect of time interval (1, 3 and 6 hours) on prophylaxis was tested, using the sulfonamides in one series and 2 percent aqueous zephiran in another. With the sulfonamides the best results were obtained at the 3-hour interval, and the poorest results at the 6-hour interval. With zephiran the results obtained at 1- and 3-hour intervals were similar, and were better than the results at the 6-hour interval.

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## **PATHOLOGY**

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### **Studies in syphilis. V. An evaluation of fibrosis and round cell infiltration of the parenchymatous organs (Warthin) in the tissue diagnosis of syphilis.**

Paul D. Rosahn and Bernard Black-Schaffer. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, 28: 142-164, Mar. 1944.

Microscopic preparations of the heart, pancreas, liver, adrenals and testes from 283 syphilitic and 722 nonsyphilitic white persons were studied in order to evaluate the histologic changes of the fibrosis and cellular infiltration which Warthin ascribed to syphilitic infection. The material for this analysis was selected from autopsies on persons aged 20 years or over performed at the Yale University department of pathology from 1917 to 1941.

No qualitative difference between the fibrosis and round cell infiltration was ob-

served in the organs of syphilitic persons and those of the nonsyphilitic controls. The distribution of these lesions and their morphologic characteristics were essentially the same in the two groups, which were indistinguishable one from the other on the basis of Warthin's criteria. The amount of fibrous replacement and the intensity of the lymphocytic and plasma cell infiltration were extremely variable in both groups, so the quantitative aspects of these changes could not be used in differentiating the syphilitic from the nonsyphilitic.

Of the 5 organs examined, the pancreas was the only one in which Warthin lesions occurred significantly more frequently among syphilitics than among nonsyphilitics. The cause of this is not clearly understood.

Comparisons were made between two groups of syphilitics, one with anatomic lesions of syphilis at autopsy, and the other with none of the morphologic changes present. The comparisons were made by means of the Chi-square test of homogeneity, and it was found that the presence or absence of syphilitic lesions was in general not a factor in the production of the tissue alterations described by Warthin.

Increasing age was found to increase the frequency of the Warthin lesions in most tissues in both groups. Other factors may also be operative, but the evidence does not support Warthin's contention that the microscopic lesion is pathognomonic of syphilitic infection.

### **General considerations on pathogenesis:**

**Syphilitic aortitis, myocarditis, hepatic cirrhosis.** Rudolf Jaffé. *J. Lab. & Clin. Med.*, St. Louis, 29: 139-149, Feb. 1944.

The author discusses the possibility that allergic phenomena play a part in the development of such diseases as syphilitic aortitis, chronic myocarditis, and hepatic cirrhosis. He found syphilitic lesions in about 17 percent of all autopsies at the Vargas Hospital in Venezuela, and these lesions were the cause of death in more than 50 percent of this group. The ratio

of males to females was 4.9 : 1, as compared with 1.7 : 1 in the nonsyphilitic patients. In 500 cases of syphilitic aortitis, the lesion was the only morphologic evidence of syphilis in most of the cases, and other organs were involved in less than 10 percent.

Syphilitic aortitis usually occurs in the first part of the ascending aorta; it may extend to the abdominal portion, and occasionally only a single isolated area is involved. The line of demarcation between the diseased and normal parts is not abrupt but fades gradually.

The author believes that the lesions in syphilitic aortitis are due to gummatous infiltrations in the adventitia and media, produced by the effects of the spirochetes in situ. Thickening of the intima and alterations of the elastic membrane are due to an allergic process. Similar changes in the aortic intima have been seen in other allergic conditions. In the course of development, the body becomes sensitized during the acute stage of syphilis, then with the reactivation of the infection new spirochetes lodge in the wall of the aorta and set up an allergic reaction in the tissue. The frequency of syphilitic aortitis seems to have increased with the use of arsphenamine. The author believes that this syphilitic aortitis may be regarded as the result of a combination of the reactions caused locally by the reactivated spirochetes and of the allergic reactions.

Chronic myocarditis is a uniform process, in which there is primarily damage to the cardiac muscle fibers and, secondarily, mesenchymal alterations, with cellular infiltrations. It is the allergic reaction of the previously damaged cardiac muscle, and has been shown to be associated with syphilis.

**Electrocardiographic patterns in cardiovascular syphilis.** Seymour L. Cole and Anne Bohning. *Am. J. M. Sc., Philadelphia*, 207: 317-331, Mar. 1944.

The electrocardiograms and postmortem findings of 30 cases of cardiovascular syphilis are presented and correlated in each case. For this purpose the electro-

cardiographic tracings were divided into several specific patterns, the criteria for which have been established.

All 30 of the hearts and aortas in this series were found to be abnormal at postmortem examination. In 8 the anatomic findings and resulting electrocardiographic tracings were entirely on a syphilitic basis. In 11 other cases, syphilitic anatomic abnormalities were combined with those of other etiologic factors to produce the electrocardiographic pattern. The remaining 11 cases manifested syphilitic lesions as coincidental findings, the electrocardiographic contours being ascribed to the nonsyphilitic lesions.

Although no specific pattern was found to be pathognomonic of syphilitic cardiovascular disease, two specific patterns occurred frequently due in whole or in part to syphilis. There were 11 cases of left ventricular preponderance and 3 cases of anterior wall infarction pattern.

The frequency of left ventricular preponderance and anterior wall infarction patterns was greatest in the cases having syphilis only, whereas nonspecific electrocardiographic abnormalities appeared when concomitant disease elements were present and nontypical patterns predominated when the latter were dominant.

Uncomplicated syphilitic aortitis, per se, and uncomplicated aneurysms caused no electrocardiographic abnormalities. Aortic regurgitation produced left ventricular hypertrophy, reflected by various types of left ventricular preponderance in the electrocardiogram.

Coronary ostial stenosis in some instances caused myocardial fibrosis which has no specific electrocardiographic pattern. Stenosis of the mouths of the coronary arteries was shown to contribute to the formation of cardiac hypertrophy, especially of the left ventricle, resulting in left ventricular preponderance patterns electrocardiographically.

When localized areas of the myocardium were deprived of their blood supply by coronary ostial encroachment, corresponding specific infarction patterns were present in the electrocardiogram. These



were all of the anterior wall type in our series. When the septum and conducting system were similarly deprived of their blood supply, the electrocardiogram showed A-V and intraventricular block.

While the absence of electrocardiographic changes does not rule out cardiovascular syphilis, most cases of far-advanced syphilis have abnormal electrocardiograms. The presence of the special patterns of left ventricular preponderance and anterior wall infarction in cases of cardiovascular syphilis uncomplicated by other diseases is a good index, respectively, of hypertrophy of the left ventricle and myocardial infarction of syphilitic origin.

**Genesis of encephalopathy due to arsphenamine (central vasoparalysis due to arsphenamine).** I. Mark Scheinker. Arch. Path., Chicago, 37: 91-98, Feb. 1944.

The author studied 5 cases of encephalopathy due to arsphenamine in which hemorrhages and typical vascular alterations were predominant. The alterations in the central nervous system in these cases consisted mainly of vascular changes typical of central vasoparalysis, associated with focal hemorrhagic and nonhemorrhagic lesions in the nerve parenchyma.

Among the underlying pathologic conditions in cases of encephalopathy due to arsphenamine are hemorrhages of different types. Those most frequently observed are minute punctuate hemorrhages distributed chiefly in the white matter, and usually occur in the forms of (1) petechial or perivascular hemorrhages filling the Virchow-Robin spaces and (2) so-called ring hemorrhages with hemorrhagic infiltration of the tissue adjacent to the vessel. In addition to these small hemorrhagic lesions, a series of nonhemorrhagic lesions may be seen in the nerve parenchyma adjacent to the smaller vessels. The different types of these lesions are described by the author, together with illustrative photomicrographs.

The vascular changes observed in the smaller veins and capillaries in these

cases and described in detail suggest a possible pathophysiologic mechanism. The widely disseminated focal lesions, both hemorrhagic and nonhemorrhagic, appear to be secondary to the vascular alterations.

In view of the vascular nature of the main alterations, the author believes the term "encephalopathy due to arsphenamine" is more appropriate than "hemorrhagic encephalitis" or "brain purpura." This term indicates that the pathologic process is not an inflammatory one and at the same time covers the vascular, hemorrhagic and nonhemorrhagic alterations of the tissue.

Two of these cases are described in detail by the author.

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## LABORATORY RESEARCH

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**Penicillin. I: Methods of Assay.** William H. Schmidt and Andrew J. Moyer. J. Bact., Baltimore, 47: 199-209, Feb. 1944.

The authors have used a modified cylinder plate procedure for the assay of penicillin.

Procedures are given for assaying penicillin by the cylinder plate and the serial dilution methods. The influence of the following factors on the former method is considered: depth of agar, stock culture of the test organisms, pH of the medium, the relationship between the rate of diffusion of penicillin and growth of the test organism, concentration of the inoculum, and condition of the ground glass surface of the cylinder.

Under the conditions used, it has been determined that it takes approximately 0.045 Oxford unit per milliliter of broth to inhibit growth of the test organism at 18 hours and 0.1 unit per milliliter of broth at 40 hours.

In an addendum, the authors say that recent studies on the stability of penicillin indicate that it is more stable at pH 6.0 than at 7.0. For that reason the pH

value of the buffer has been lowered from 7.0 to 6.0. Solutions of  $\text{KH}_2\text{PO}_4$  and  $\text{K}_2\text{HPO}_4$ , each containing 1 percent salts, are mixed in such a proportion to give a final pH of 6.0. This buffer is used only for making dilutions and is not used in making Medium II. It is kept saturated with toluene and chloroform at all times.

**Further study of the chick embryo as a culture medium for the *Spirochaeta pallida*.** Udo J. Wile and Sture A. M. Johnson. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, 28: 187-191, Mar. 1944.

Five experiments were done using 2 to 3 dozens of 11- to 12-day-old developing chick embryos which had been incubated at 38° C. as media for *Spirochaeta pallida*. One experiment was successful. Two rabbits, inoculated from the same darkfield negative chorioallantoic membranes and embryo tissues, developed serologic and physical evidence of syphilitic infection. In both animals the Kahn standard reaction was positive and the Kahn quantitative reaction was 128 units after 77 days, and the firm swollen testicles contained many motile *S. pallida*. An emulsion of isotonic solution of sodium chloride and ground testicular material from one of the rabbits caused typical syphilitic infections and Kahn reactions in 4 rabbit generations; the other, in 5 rabbit generations. In all, 22 rabbits have been successfully inoculated without a single failure taking place.

The positive result from one testicle of the rabbit after 53 days of incubation and the negative result from the other testicle after 61 days suggest an optimum time for successful inoculation.

**Action of sulfonamides on toxins of agents of the lymphogranuloma-psittacosis group.** Geoffrey Rake and Dorothy M. Hamre. *Proc. Soc. Exper. Biol. & Med.*, Utica, 55: 90-91, Feb. 1944.

The authors have shown elsewhere that the agents of the lymphogranuloma-psittacosis group so far investigated produce a rapidly lethal toxin which re-

sembles the bacterial endotoxins. Following the earliest report on the existence of these toxins the question has been raised as to how to be sure that a toxin and not an infection which was acting very rapidly was being dealt with.

Experiments were set up with 3 agents showing the 3 different types of response, namely, lymphogranuloma venereum, mouse pneumonitis, and feline pneumonitis. The results are shown in a table and completely confirm the theories outlined. It was found that sulfamerazine has no effect on any of the endotoxins of the agents of the lymphogranuloma-psittacosis group and on the early deaths produced by such toxins, even when these are used in doses on the border line of lethality and are derived from lymphogranuloma venereum or mouse pneumonitis, both of which infections are very susceptible to sulfonamide therapy.

**Observations on the detection of the gonococcus by culture methods.** Charles E. Lankford. (*Proc. Texas Br., Soc. Am. Bact.*) *J. Bact.*, Baltimore, 47: 217-218, Feb. 1944.

Studies with proteose peptone No. 3-hemoglobin agar (Bacto) indicate that it is not equally productive for all strains of gonococci. The addition of 5 mg. percent cystine markedly increases colony size of many strains, and the same effect is obtained with 5 mg. percent cysteine, 10 mg. percent glutathione, or 400 mg. percent Bacto Yeast Extract, but not with methionine or thioglycollate.

Glutamine, already reported as a growth factor for about 10 percent of gonococcic strains, is not supplied by the medium and must be added as a filtered or toluene-preserved supplement to a final concentration of 0.2 mg. percent glutamine (fresh) or 1 percent beef extract. Glutamine is destroyed completely when autoclaved with agar base. Solid glutamine should be stored in a desiccator at low temperature.

Certain strains of gonococci require a "thermostable" factor which is not supplied regularly by the base medium. Yeast extract is highly active in promot-



ing growth of these strains; its activity is largely destroyed by sulfite or by alkaline autoclaving. Yeast extract is replaceable by 0.5 gm. percent thiamine hydrochloride, but evidence indicates a more active form of the factor in the extract. Like the glutamine-deficient type, these strains readily produce variants capable of synthesizing this factor.

**A solid medium for the transportation of delayed gonococcus cultures.** Nell Hirschberg. *J Lab. & Clin. Med.*, St. Louis, 29: 314-318, Mar. 1944.

North Carolina is a rural State; from many communities it takes 2 or 3 days for specimens for diagnosis to reach the laboratory at Raleigh. It was necessary, therefore, to develop a solid medium for the transportation of gonococcus specimens for culture. After experiments with various mediums the author has developed the following as the most suitable: Proteose-agar concentration No. 3 (Difco), 4.5 percent plus additional shredded plain agar to make a final concentration of 2 percent, 4 percent gelatin, 0.24 percent Nile blue A, and 20 percent chocolate blood. The medium is very smooth, easy to penetrate with a swab, and supports the growth of the gonococcus luxuriantly.

Cultures and spreads were taken as patients were examined in the routine Friday night Asheville gonorrheal clinic. The tubes were mailed to the Raleigh laboratory the next morning and the specimens were usually cultured Monday afternoon, approximately 3 days after swabs had been taken. The swabs were streaked onto Peizer's medium and onto chocolate agar plates. After 48 hours, the plates were examined by means of the oxidase reaction and gram-stained spreads. The results obtained in Raleigh were checked with controls in Asheville.

The results in a series of 142 cases are reported. Those specimens of which culture was made immediately gave 88 negative and 54 positive, and the delayed cultures resulted in 91 negative and 51 positive, the delay in culture being from 1 to 5 days.

**Studies on the gonococcus. I. Constitution of the cell. II. Properties of an antigen fraction isolated from cell-free gonococcal broth supernatants.** Herbert E. Stokinger, Helen Ackerman and Charles M. Carpenter. *J. Bact.*, Baltimore, 47: 129-139, 141-147, Feb. 1944.

I. Microchemical analyses were carried out on 6 strains of *Neisseria gonorrhoeae* grown in Douglas's broth. Data are presented on 19 components of the cell. Carbohydrate constituted from 5 to 9 percent of the weight of the dried cell, lipid from 10 to 14 percent, and nucleoprotein from 60 to 65 percent. Volatile and nonvolatile matter constituted an additional 13 to 18 percent. Comparative analyses on cultures grown for 3, 6 and 10 days showed that phosphorus-containing constituents, chiefly nucleic acid and phospholipid, are reduced to one-half this maximal value between the third and sixth day. No such change was noted in the nitrogenous components, notably protein, certain amino acids, nitrogenous lipid, and amino sugar.

Two nucleoprotein fractions have been isolated, analyzed, and a number of their properties described. Of chief importance was the characterization of a relatively insoluble liponucleoprotein containing approximately 25 percent bound lipid and a minor lipid-free soluble nucleoprotein which constituted the major part of the gonococcal cell.

The lipid which was recovered was highly complex. It was separated into several crystalline and noncrystalline substances, certain of which were identified as a lecithin, a cephalin and a sphingomyelin. No lipid constituent characteristic of the gonococcus was obtained.

It was not possible to demonstrate by chemical methods of analysis or of isolation the presence of a type-specific polysaccharide in the gonococcal cell grown in Douglas's broth.

II. A protein-like fraction, possessing "toxic" and antigenic properties, was separated from broth cultures of *Neisseria gonorrhoeae* after removal of the cells by centrifugation. The fraction appeared to

be a protein degradation product derived from the nucleoprotein of the cells. This conclusion is based upon its destruction by proteolytic enzymes, by reversible loss of complement-fixing activity after treatment with protein denaturants, by its peculiar immunologic behavior in specific antisera, and finally, by chemical analyses.

The purified fraction fixed complement in the presence of sera from rabbits immunized with *Neisseria gonorrhoeae* and of sera from patients with gonococcal infection.

The toxicity of the fraction for laboratory animals was greater than that of nucleoprotein of the cells. The MLD<sub>100</sub> of several preparations varied from 0.1 to 0.7 mg. for white mice weighing from 20 to 22 gm.

The major component of the purified fraction consisted of molecules with similar electrophoretic behavior and antigenic activity. The minor component was rich in carbohydrate and nonantigenic.

**Studies on the gonococcus. III. Quantitative agglutinative reactions of the *Neisseria* with special reference to *Neisseria gonorrhoeae*.** Herbert E. Stokinger, Charles M. Carpenter and Jane Plack. *J. Bact.*, Baltimore, 47: 149-157, Feb. 1944.

A measure of the immunologic interrelationships of *Neisseria* has been obtained by use of a modified quantitative agglutinative technic, based on those of Heidelberger and Kabat. The adaptation of these methods, shown to be necessary in the case of *Neisseria gonorrhoeae*, consisted in carrying out the reaction at pH 5.9. At this pH the solubility of certain antigenic constituents of the gonococcal cell was minimized, and the maximal amount of agglutinin was recovered.

A study of 9 strains of *Neisseria gonorrhoeae* isolated from various types of gonococcal infection and maintained under artificial cultivation for from 1 month to 34 years failed to show any evidence of distinct types or groups. There was a closer immunologic relationship between certain strains of *Neisseria intracellu-*

*laris* and *Neisseria gonorrhoeae* than among certain strains of the latter species.

**A simple rapid test for detection of sulfonamide compounds in urine: A preliminary report.** Robert Hubata. *War Med.*, Chicago, 5: 56-57, Jan. 1944.

The author has devised a simple rapid test for the detection of sulfonamide compounds in the urine which requires the use of only one chemical; measurement of the reagent from buret or pipet is not necessary, nor is timing interval or filtration or dilution of the specimen required. The method is based on the color reaction in the presence of acids between crude cellulose (newspaper, matchsticks, pine shavings) and the arylamine group, as described by Hallay in 1942. A small area on a blank strip of newspaper is moistened with a drop or two of the specimen to be examined, and a small drop of dilute hydrochloric acid (1:4) is then placed on the center of the moistened area. The immediate appearance of a yellow to orange color indicates the presence of a sulfonamide compound. Refined pulp paper will not give the reaction.

Tests were made on a number of specimens of urine from hospitalized persons and the results are shown in tables. Specimens from 28 normal persons were also tested by the same methods with negative results in all instances. Specimens from persons who had recently discontinued taking a sulfonamide compound gave a yellow color, which was considered a 1 plus positive reaction.

**Quantitative studies of sulfonamide inhibitors.** Lowell A. Rantz and William M. M. Kirby. *J. Immunol.*, Baltimore, 48: 29-37, Jan 1944.

The effects of peptone, yeast extract, various amino acids, glucose, and the temperature of incubation on sulfonamide bacteriostasis were studied. The studied "sulfonamide inhibitors" were shown to have two effects on bacteriostasis. Peptones improve the environment of the organism and thus in a non-



specific manner interfere with sulfonamide action. The work of Cooper and Kellar and the experiments described in this report, in which the temperature of incubation markedly affected bacteriostasis, indicate that the improvement of a suboptimal bacterial environment may be expected to reduce the effectiveness of a sulfonamide. Yeast also enhances the ability of the test-organism to grow. Certain substances, which eliminate or impair bacteriostasis without augmenting the rate of bacterial growth in controls, were true sulfonamide inhibitors. Para-aminobenzoic acid is the most important of these.

In conclusion, the authors say that the results of their experiments and the observations of others indicate that there are three types of sulfonamide "inhibitors": those that interfere with the action of sulfonamides at their primary site of action in the enzyme requiring para-aminobenzoic acid; those whose presence in increased concentration permits bacterial growth even though the primary system is partially blocked, presumably by supplying ready-made the end products of the para-aminobenzoic acid enzyme, and those whose action is largely dependent upon their ability to improve the environment of the organism and thus its resistance to the bacteriostatic action of the sulfonamides.

**Demonstration of sulfonamide inhibitor production by bacteria on agar containing sulfonamide.** Robert M. Pike and Alice Zimmerman Foster. *J. Bact.*, Baltimore, 47: 97-105, Jan. 1944.

The production of extracellular sulfonamide-inhibiting substances by bacteria was demonstrated by appropriate solid media containing sulfonamide by observing the ability of a heavy, concentrated inoculum to make possible the growth of a lighter dispersed inoculum of the same or another strain which would otherwise be inhibited. The resulting formation of satellite colonies depended upon the concentration and bacteriostatic power of the sulfonamide used and the susceptibility of the satellite

strain. Highly resistant bacteria did not necessarily stimulate satellite formation. In general, the ability of a micro-organism to induce satellite growth was associated with its production of extracellular sulfonamide inhibitor.

**Correlation of in vitro resistance and clinical response of the gonococcus to sulfonamides.** Charles E. Lankford, Willard R. Cooke, Priscilla Kringle and Sara Malone. (*Proc. Texas Br., Soc. Am. Bact.*) *J. Bact.*, Baltimore, 47: 217, Feb. 1944.

The in vitro tolerance of over 2,000 strains of gonococci from 367 female infections has been studied and found to fall into a typical distribution curve within the limits of 0.5 to 40,000 microgram percent sulfathiazole. A significant increase within the past 14 months was observed, corresponding to an increase in sulfathiazole-resistant infections.

Comparison of in vitro tests and clinical results of sulfathiazole therapy points to the following types of response: (1) Sensitive strain and responsive infection; (2) initially resistant strain and resistant infection, probably acquired from resistant contact; (3) sensitive strain and resistant infection, with chronic salpingitis a frequent feature; (4) initially sensitive strain which increases in tolerance from 10- to 1000-fold during treatment, the patient showing an initial temporary therapeutic response; (5) loss of strain resistance, or acquisition of resistance with subsequent reversion to sensitivity, with corresponding clinical response, a phenomenon which has been duplicated in vitro; (6) miscellaneous types of response. The clinical and bacteriologic characteristics of each type of response were described.

**The velocities of inhibition of bacterial growth by sulfonamide and of the antagonistic effect by p-aminobenzoic acid.** Julius Hirsch. *J. Immunol.*, Baltimore, 48: 199-201, Mar. 1944.

Prior to the introduction of sulfonamides, chemotherapeutic agents were looked upon as cellular poisons which

caused death, or at least inhibition of growth, by damage to the protoplasm of the bacterial cell. The exploration of the mechanism by which sulfonamides take effect has demonstrated that antibacterial effects can be obtained without general damage to the cells, especially by disturbance of the assimilatory process connected with multiplication. This development entailed a change in methods of in vitro investigation of chemotherapeutic agents.

The author discusses two experiments, A: sulfonamide effect, and B: the effect of p-aminobenzoic acid. He says that on the basis of his observations, the interference with the action of p-aminobenzoic acid by sulfonamides postulated by Fildes and the experimentally demonstrable interference with the sulfonamide effect by p-aminobenzoic acid cannot be considered as equivalent processes caused by a similar reversible action. This is more evident if the concentrations of the participating substances are considered. In experiment B, inhibition of growth was instantly antagonized by a concentration-ratio of 1 mol of p-aminobenzoic acid to 10 mol of irgafen ( $N_1$ -3, 4-dimethylbenzoylsulfanimamid). No definite statements can be made concerning the concentration-ratios of the two competitors in the inhibitive experiment A.

It was found that the inhibiting effect of sulfonamide has a lag-period of 1 to 2 hours; in contrast to this, the bacteriostatic effect of sulfonamide is instantly antagonized by addition of p-aminobenzoic acid.

The findings suggest that the inhibition of bacterial proliferation by sulfonamides is a more complex process than the reversal of inhibition by p-aminobenzoic acid.

**Sulfonamide inhibiting action of procaine.** Osler L. Peterson and Maxwell Finland. *Am. J. M. Sc.*, Philadelphia, 207: 166-175, Feb. 1944.

The authors carried out experiments both in vitro and in vivo on the antisulfonamide action of procaine in human serum. Their conclusions were that pro-

caine, in amounts ordinarily employed for local anesthesia, may be absorbed into the circulation in sufficient concentration to exert inhibiting effect on the action of sulfonamide drugs that may be present in the blood. Infection introduced into an area which has been infiltrated with procaine may become established locally in spite of the continuous presence in the body of bacteriostatic concentrations of sulfonamide drugs.

The authors believe that local anesthetic drugs other than p-aminobenzoic acid derivatives should be used for infiltration when performing exploratory punctures of potentially infected areas. Procaine, or similar anesthetics of the p-aminobenzoic acid series, should also be avoided in extensive procedures on patients having severe infections in which rapid and effective action of sulfonamide drugs is essential.

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## **PUBLIC HEALTH ADMINISTRATION**

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**To attack delinquency: A seven-point program.** Charles P. Taft. *J. Social Hyg.*, New York, 29: 485-491, Nov. 1943.

In launching a fresh attack on delinquency the author suggests seven points around which to center such a program. The points suggested are good family life, good education and day care, good recreation, good health and mental hygiene, sound law enforcement, social protection and employment safeguards for young workers.

The Social Protection Division of the Office of Community War Services is helping communities in many ways. It is concerned with the suppression of commercial prostitution and the protection of young girls from becoming involved in prostitution or promiscuity. In the work of redirecting and rehabilitating delinquent girls, the division helps communities to provide the special skills and facilities needed, which includes medical treatment for the girl infected with ve-



ereal disease. The United States Public Health Service is expanding these rehabilitation services all over the country. In the end it is the community which must help the girl to find her place in life by offering her a normal social life and employment if she is old enough.

Although the primary responsibility in meeting the problem of juvenile delinquency lies with the community, the Federal government can do its part. It has three things to offer in meeting these problems: leadership, funds, and trained technical consultants.

**Recommendations regarding the teaching of facts concerning the venereal diseases at the secondary-school level.** California's Health, Sacramento, 1: 80-81, Dec. 15, 1943.

Since the approach to venereal disease education as a part of the health education program at the secondary-school level should be based on the two considerations of immediate wartime necessity and the long-range program, the National Conference for Cooperation in Health Education, New York, April 1943, recommended: (1) Definite procedures looking toward adequate venereal disease educational content in health and physical fitness programs in the secondary schools and teacher-education institutions; (2) forming of a research committee to study past experiences in venereal disease education in secondary schools, to evaluate these experiences, and to formulate a program for consideration of health officers and educators at Federal, State, and local levels.

The Committee on Teaching the Facts About the Venereal Diseases at the Secondary-School Level suggested that the following requirements be considered in shaping the wartime program:

(1) That venereal disease education be included as an integral part of the health and physical fitness programs in secondary schools throughout the country.

(2) That the U. S. Public Health Service and the U. S. Office of Education recommend appropriate teaching methods

and materials, and that these suggestions be available to health departments and school officials in the various States.

(3) That State and local health departments be asked to cooperate with State departments of education and local school systems in preparing and providing materials to teachers.

(4) That the assistance and advice of voluntary agencies be sought.

(5) That the Secretary of War, the Secretary of the Navy, and the War Manpower Commissioner be asked to endorse this venereal disease education program in view of its wartime character.

In the long-range program, to insure that effective methods and materials developed during the war will be further developed and utilized during peacetime, it is recommended:

(1) That a research and planning subcommittee be named to formulate a long-range teaching program.

(2) That to facilitate the work of the subcommittee, the U. S. Public Health Service and the U. S. Office of Education assign personnel to collect and study experiences of similar programs.

(3) That, based on the data assembled, a program of teaching recommendations be submitted for analysis and approval.

(4) That steps be taken by the Conference to encourage pre-service and in-service preparation of educators.

**Sex education.** London correspondent. J. A. M. A., Chicago, 124: 726, Mar. 11, 1944.

Since the tendency of wartime is to break down restraints, the need for young people to be suitably introduced to and instructed in matters of sex and the responsibility of the schools and youth organizations in this work are increased. The Board of Education has therefore issued a pamphlet on sex education in schools and youth organizations which asks particular attention of local authorities to two possibilities: (1) short courses on sex education for teachers and youth leaders, and (2) the organization of parents' meetings, with a view to securing their cooperation in anything done

through the schools and helping them to deal with their own children.

Whatever questions are asked by the child and at whatever age the child asks questions concerning human reproduction, the answer should be given to the fullest extent that the child can understand. Since a substantial proportion of parents are reluctant to do this, there is the need for instruction in school, with special attention being given to venereal diseases.

The age at which sex instruction is given varies, the most common age being 13 years, the stage at which mammals and man are most often discussed in biology courses. A girls' organization has suggested, as being most successful in giving such instruction, "a really good woman physician, preferably married, youngish, with a modern approach and modern clothes."

**First 2,000,000 selectees blood tested for syphilis.** Georgia's Health, Hapeville, 24: 1, 3, Feb. 1944.

According to Selective Service rates, Georgia stands third in the Nation, with a rate of 145 out of every 1,000 male population of draft age having syphilis.

Considering the short time an intensive venereal disease control program has been in force in the State, great progress has been made. There are 267 venereal disease clinics operating in 147 counties, and approximately 45,000 individuals with syphilis now under active treatment. Two special treatment centers, one in Augusta and one in Savannah, have been established. Two recent laws, one to better suppress prostitution and the other to require all expectant mothers to have a blood test, have given new strength to the fight. The civic organizations have been giving more support to the control program.

**Medical progress: Syphilis.** G. Marshall Crawford. New England J. Med., Boston, 230: 109-114 and 138-145, Jan. 27 and Feb. 3, 1944.

This is an extensive review of recent publications on syphilis, based on 71 refer-

ences appearing in the literature during 1941, 1942 and 1943.

This report covers the public health aspect, experimental research, pathology, morphologic diagnosis, and reinfection of syphilis. Syphilis in the Armed Forces, in industry, and its prevalence with cancer are included.

The clinical problems discussed include syphilis in blood donors, false positive serologic reactions following smallpox vaccination, syphilitic spondylitis, neurosyphilis, and congenital syphilis, together with treatment recommended and reactions which may result from therapy.

The author comments on the failure to follow up blood donors who have been found to have a positive serologic test for syphilis and believes that some provision should be made for a follow-up of these cases. The use of penicillin and the experimental use of arsenical drugs by intramuscular and oral administration in the treatment of syphilis offer hopeful advances in the field of therapy.

**Ophthalmia neonatorum.** Eric Assinder. Brit. J. Ven. Dis., London, 19: 173-179, Dec. 1943.

The author, who is director of the venereal diseases department of the Birmingham General Hospital, states that the notification of ophthalmia neonatorum should be made more general throughout the country. A purulent discharge, however slight, occurring in an infant up to 3 weeks of age should be reported as ophthalmia neonatorum, and it should not be a matter for differentiation. The city of Birmingham encourages the doctors and midwives to report these cases and to send them for diagnosis and treatment to a central depot. As a result, Birmingham accounted for nearly one-quarter of the total cases from the whole country.

A survey of the years 1934 and 1941 shows gonococci were responsible for ophthalmia neonatorum in approximately 1.8 percent of the reported cases in 1934, as compared with 0.86 percent in 1941. Up to September 1943 there has been no increase in the number of cases of gonococcic ophthalmia neonatorum. The au-



nor states that ordinarily an increase could be seen due to war conditions, but that the general use of sulfonamides in pregnant women with gonorrhea has decreased this condition.

A general outline of treatment is given.

The author recommends that a central clinic with a visiting staff be set up in all large towns and be available to patients from the surrounding districts, that a bacteriologic investigation be made in every case, and that treatment be commenced early.

**Report of an outbreak of gonorrhea at a boys' school.** Robert S. Westphal. New York State J. Med., New York 44: 493-496, Mar. 1, 1944.

The author reports an outbreak of gonorrhea in a Negro boys' school, which occurred between Dec. 20, 1942 and Jan. 13, 1943. The school was established for the rehabilitation of Negro boys who had committed misdemeanors or who were underprivileged in their home environment. The ages of these boys ranged from 9 to 16 years, with 84 percent being between 10 and 13 years of age.

There was a total of 17 (25.4 percent) cases of gonococcic infection among a total of 67 boys. Of these 17 cases, 6 were confirmed by laboratory tests; in 6 the diagnosis was made upon history and clinical evidence, and in 5 on clinical evidence alone.

The initial case had contacted the infection 15 days before while home on vacation. The remainder had contracted their infection from contact with patients who had gonococcal proctitis. In the course of investigation it was discovered that sodomy was practiced generally among the boys. Examination of all the boys was made. Because of the possibility of the existence of symptomless carriers, and in order to prevent any further spread of the infection by such individuals, it was decided to administer sulfathiazole to all members of the school. Two grams of sulfathiazole daily by mouth for 10 days proved to be adequate for controlling the infections and for prevention of further spread.

**Administration of a Provincial venereal-disease control program.** Elphege Lalande and Jules Archambault. Canad. J. Pub. Health, Toronto, 35: 55-58, Feb. 1944.

The National Venereal Disease Control Conference, held in Ottawa, December 1943, was for the purpose of considering how existing facilities for the prevention of venereal disease may best be utilized in Canada, and what is needed in the way of modification and extension of these facilities.

The authors present a summary of the measures adopted by the Division of Venereal Disease and suggest modifications or extensions of the existing facilities. Included in this summary are reporting of cases, case finding, epidemiologic approach, treatment of patients, law enforcement and education.

In addition to the already organized venereal disease program, the authors further recommend:

1. That, by effective tracing of contacts of recent venereal disease infections, evidence of the activities of prostitutes be collected, and that the Venereal Disease Division instruct the law-enforcing agencies in the proper action to be taken with respect to these sources of infection.
2. That the main and constant effort be directed toward educating the public, the medical profession, and others concerned.
3. That the law-enforcing agencies extend to the Division of Venereal Disease all the cooperation and assistance required.
4. That specific laws be enforced against those who participate in or exploit prostitution, that appropriate action be instituted to remove those conditions which facilitate association of prostitutes and healthy persons, and that proceedings against prostitution be taken by Federal police, when necessary.
5. That serious thought be given to the possible rehabilitation of prostitutes.
6. That a large share of the instruction given by universities be devoted to

venereal diseases and their epidemiologic aspects.

7. That blood testing be made compulsory for persons contemplating marriage and for pregnant women.

8. That the Federal Division of Venereal Disease Control in the Department of Pensions and National Health be maintained permanently in order to assist the Provinces in their various problems of venereal disease control as well as financially.

#### Campaign against yaws in Venezuela.

(La campaña contra la buba en Venezuela.) Martin Vegas, Ildemaro Lovera, Pedro Miguel Itriago and Rafael Medina. *Rev. san. y as. soc.*, Caracas, 8: 1015-1061, Oct. 1943.

A campaign against yaws was initiated in Venezuela in September 1938, inspired by the work carried out in Jamaica by the Rockefeller Foundation. Vegas was appointed Chief of the Division of Syphilography, Dermatology and Leprosy, and commissions and subcommissions took up the work in the Yargas district and 7 States. Good cooperation was obtained from local authorities, and some States gave financial aid.

It was extremely difficult to determine the prevalence of the disease because of the nature of the country—great distances, mountainous terrain, impassable roads, the rainy season—and the nomadic nature of the inhabitants, and their reluctance to meet strangers.

The cases were divided into two types: (1) Those with early lesions of less than 5 years' duration and without actual clinical manifestations of the disease, and (2) those with infections of more than 5 years' duration, and with clinical manifestations. The contacts were classified into the two groups of those who had not had yaws and those who had had. In the latter group were those whose disease was of more than 5 years' duration without having caused clinical manifestations and those whose disease was of less than 5 years but who had received specific therapy which the commission's examining physician considered adequate.

For treatment the commission furnished a liposoluble bismuth preparation through the year 1941 and thereafter an insoluble bismuth preparation. It also furnished an antiseptic ointment consisting of yellow oxide of mercury, 2 percent; iron subcarbonate, 5 percent; balsam of Peru, 10 percent, and vaseline. The purpose of the ointment was to stimulate cicatrization of lesions and to cover the contagious lesions.

A house in the community, or several houses if necessary, was fitted as a treatment center. Each patient received 6 injections of bismuth in the course of 3 to 5 weeks, the dosage being determined by examination of the urine for albumin. It was impossible to do routine Kahn tests because of the unfavorable conditions under which the work had to be carried out. The treatment of infectious cases was made absolutely obligatory; they were isolated until treatment had been completed. Treatment was given also to persons having skin lesions of various kinds or wounds who have to come in contact with yaws patients.

The Central Commission studied a total of 39,761 cases of yaws and contacts at 7,537 treatment centers. These cases were classified as follows: (1) Cases of yaws: (a) actual cases, contagious 2,194 (5.52 percent), noncontagious 1,637 (4.11 percent), (b) old cases, 5,932 (14.92 percent); (2) Contacts: (a) in the home 2,888 (7.26 percent), outside of the home 27,110 (68.18 percent).

Of the contagious cases, 1,574 (71.7 percent) were found among children under 15 years of age. There were 381 contagious cases in the age group of 15 to 24, 163 between 25 and 39 years of age, 76 over 40 years.

In the district of Bejuma and the State of Carabobo, of 11,108 persons examined, 2,155 (19.4 percent) were found to be infected. Of these, 1,265 had a history of the disease, 437 were in the contagious stage, and 453 were no longer contagious. The greatest number of infections were found in the State of Miranda; there was 9.85 percent noncontagious cases and 24 percent who had had the disease but



did not require treatment. In Tacarigua the contagious and noncontagious cases were 17.57 and 11.81 percent, respectively; in the Acevedo district 12.33 and 14.12, and the old cases 33.17; other districts varied between 2.54 and 7.56 for contagious cases, between 1.89 and 7.14 for noncontagious, and for all types between 7.93 and 32.71.

**Prevalence and incidence of syphilis in Venezuela.** (Prevalencia e incidencia de la sífilis en Venezuela.) Rev. san. y as. soc., Caracas, 8: 961-966, Oct. 1943.

Routine serologic Kahn tests carried out on members of various groups of people at the Division of Venereology showed the following positive results: Among 51,049 workers who applied for health certificates, 9,069 (17.7 percent) (among miners—numbers not given—from 27 to 50 percent); of 12,291 pregnant women, 1,936 (15 percent); of 6,491 prostitutes, 3,812 (58.7 percent); of 5,718 soldiers, 1,859 (32.5 percent); of 3,508 students in the interior (not known whether these were routine tests), 227 (6 percent); of 1,515 children in Caracas, 3.7 percent.

The antivenereal clinics in Tovar, Puerto Cabello, La Guaira, Maracaibo and Merida reported that they had obtained 275 positive Kahn blood tests on samples of blood obtained from 684 farmers (41.95 percent); the author expresses doubt that these people were really farmers. Carlos Abreu, who examined 150 persons in a truly rural environment, found 4 percent positive blood serologic reactions (type of test not indicated).

The author estimates that 10 percent of the population of Venezuela has syphilis.

**Present experience in the campaign against syphilis.** (La experiencia de hoy en la lucha antisifilítica.) Juan Gambús. Rev. san. y as. soc., Caracas, 8: 967-971, Oct. 1943.

During the past year the Division of Venereology has been able for the first

time to estimate the incidence of syphilis in the 51 population groups of the country which have antivenereal disease clinics. At these clinics a total of 5,599 patients with early syphilis were registered. In terms of the total population of these cities of approximately one million inhabitants the annual incidence is 559 cases per 100,000 inhabitants.

Venezuela furnishes free and obligatory treatment for syphilis, has systematic examination of prenatal cases, obligatory reporting, investigation of contacts, and follow-up of persons who abandon treatment. Hospitals are obliged to furnish beds for syphilitic patients in the infectious stages. Venezuela also requires health certificates, prohibits the practice of medicine by quacks, and the sale of antisiphilitic drugs without prescription. The intensive treatment of syphilis is being studied at the present time.

**Annual Report for 1942. II. Venereal diseases.** Bol. san. argent., Buenos Aires, 7: 61-65, 1943.

The antivenereal disease program initiated in 1938 was continued and elaborated during 1942. The number of clinics increased from 717 in 1941 to 745 in 1942; of these 44 are directly dependent upon the National Health Department. That department has furnished the treatment centers with arsenical drugs, bismuth, and mercury preparations. The Chemical and Bacteriologic Institute has continued its valuable collaboration and has increased its manufacture of drugs and vaccines in order to supply the increasing demand for these products.

According to monthly statistical reports received from the centers, there was a slight increase in the number of cases of early syphilis and of gonorrhea. This is attributed to laxity in the suppression of clandestine prostitution.

Antivenereal disease propaganda has been continued.

# New Cases of Syphilis and Gonorrhea in States, Territories, and Possessions

Health officers' monthly statement: Reported for the first 8 months of fiscal years 1943-44 and 1942-43

Area	Cases of syphilis and gonorrhea reported for first 8 months of fiscal years below											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital			
	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43
United States†	1302,842	1368,927	250,760	254,420	281,498	296,385	2132,215	2164,779	28,753	210,887	2192,934	2176,977
Alabama-----	11,650	14,512	1,562	2,343	2,679	4,042	2,730	4,385	245	357	4,334	6,059
Arizona-----	1,853	1,524	432	215	504	325	725	868	87	60	1,139	600
Arkansas-----	6,735	11,126	841	1,225	2,250	4,262	2,597	4,508	144	170	3,033	3,278
California-----	21,561	19,298	3,473	2,679	5,013	4,181	12,048	11,120	639	551	22,023	14,822
Colorado-----	2,787	2,981	678	570	790	692	1,212	1,588	107	131	2,219	1,531
Connecticut-----	1,895	1,816	224	174	838	550	480	640	71	68	1,046	984
Delaware-----	634	724	94	89	161	171	145	197	9	20	147	112
Dist. Columbia-----	5,556	(*)	639	(*)	1,316	(*)	3,349	(*)	90	(*)	2,516	(*)
Florida-----	19,330	23,061	2,189	2,850	6,090	5,690	8,800	11,717	406	531	10,839	8,807
Georgia-----	10,537	18,890	2,068	2,592	4,249	8,885	3,904	6,899	311	513	6,778	8,600
Idaho-----	356	307	162	96	61	19	102	149	5	15	547	212
Illinois-----	18,483	19,554	2,495	2,240	4,243	3,926	11,377	12,886	368	502	15,651	13,213
Indiana-----	5,828	9,263	886	1,175	530	197	2,144	3,601	163	305	2,463	3,012
Iowa-----	1,639	1,953	319	226	432	626	710	883	110	70	1,195	1,213
Kansas-----	1,918	2,637	391	549	405	289	1,052	1,210	70	79	1,264	1,800
Kentucky-----	4,754	9,220	751	1,104	1,032	1,923	2,002	3,956	181	293	2,364	3,040
Louisiana-----	11,870	12,468	1,987	1,718	3,062	3,578	3,109	5,951	298	352	9,120	4,239
Maine-----	589	601	130	135	86	87	290	270	48	61	899	470
Maryland-----	9,851	11,875	1,094	839	1,045	990	1,909	1,428	83	142	4,807	5,454
Massachusetts-----	3,726	3,638	764	627	(§)	(§)	2,748	2,840	212	169	3,358	3,095
Michigan-----	11,322	8,752	1,673	1,218	2,920	1,858	4,833	3,884	283	316	7,423	5,845
Minnesota-----	1,629	2,042	156	148	174	216	1,187	1,562	81	72	1,290	1,033
Mississippi-----	17,311	27,364	5,874	6,704	4,852	9,294	5,868	10,357	713	1,009	19,738	22,314
Missouri-----	6,855	6,817	1,176	1,045	1,764	1,376	3,323	3,280	224	175	3,846	3,005
Montana-----	283	342	71	110	49	24	114	161	5	6	208	222
Nebraska-----	843	1,476	127	164	398	345	256	889	24	47	1,000	1,171
Nevada-----	487	537	15	(*)	94	(*)	336	(*)	17	(*)	249	182
N. Hampshire-----	162	219	23	23	37	19	86	147	7	18	131	131
New Jersey-----	7,394	7,546	866	913	2,272	1,922	3,943	4,377	294	254	3,615	4,581
New Mexico-----	1,303	1,593	269	263	302	311	671	837	60	74	955	446
New York-----	24,488	24,567	3,542	2,466	4,285	3,868	15,678	17,688	672	847	12,860	10,625
N. Carolina-----	7,525	12,253	1,952	2,531	3,078	5,070	2,365	4,341	130	311	5,979	7,357
North Dakota-----	206	229	71	30	33	37	58	103	13	13	177	170
Ohio-----	15,394	15,695	2,398	2,228	3,713	3,615	7,889	9,169	613	683	3,633	3,147
Oklahoma-----	5,298	6,792	699	1,034	1,495	2,501	1,940	1,723	199	185	3,392	3,008
Oregon-----	1,357	975	418	183	108	93	786	624	45	58	1,662	850
Pennsylvania-----	8,898	3,891	1,188	757	3,368	2,489	3,301	266	442	63	(*)	(*)
Rhode Island-----	703	769	56	29	73	62	502	588	17	27	504	344
S. Carolina-----	10,849	13,405	2,189	2,764	4,384	5,572	3,768	4,589	264	295	4,509	3,785
South Dakota-----	340	343	63	64	60	126	164	124	27	14	255	202
Tennessee-----	12,611	16,415	1,638	2,073	5,091	5,417	5,458	8,358	272	388	9,725	7,292
Texas-----	16,983	33,719	2,104	3,597	5,163	6,672	7,030	10,568	503	1,245	7,330	12,077
Utah-----	569	412	143	134	74	46	340	220	12	8	409	544
Vermont-----	169	182	54	97	51	0	56	77	7	8	135	124
Virginia-----	9,915	12,315	2,820	3,584	3,760	4,343	3,010	3,957	183	242	8,296	5,551
Washington-----	2,921	(*)	590	(*)	634	(*)	1,297	(*)	91	(*)	5,723	(*)
West Virginia-----	2,484	3,888	456	578	407	665	586	1,105	79	123	1,529	1,641
Wisconsin-----	625	725	118	146	0	1	500	567	7	12	729	537
Wyoming-----	843	306	76	91	117	10	419	122	20	5	129	252
<i>Territories and possessions</i>												
Alaska-----	65	113	39	24	13	31	10	32	1	5	297	362
Hawaii-----	641	768	120	216	74	91	446	377	39	37	1,137	972
Puerto Rico-----	10,073	6,137	1,046	1,367	1,980	901	3,349	2,156	1,288	1,081	2,513	1,985
Virgin Islands-----	145	144	26	35	86	82	26	21	6	6	219	95
Actual total of U. S. and possessions†	322,243	376,089	53,235	56,062	85,695	97,490	141,028	167,365	10,285	12,016	205,339	180,391

\*Data not available.

\*\*Includes "Not Stated."

†Based on States reporting in both fiscal periods.

‡Includes all reported cases.

§Included in late and late latent.

1 Based on 47 States.

2 Based on 46 States.



# New Cases of Syphilis and Gonorrhea in Cities of 200,000 Population and Over

Health officers' monthly statement: Reported for the first 8 months of fiscal years 1943-44 and 1942-43

City	Cases of syphilis and gonorrhea reported for first 8 months of fiscal years below											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital			
	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43
Total†-----	110,354	111,308	12,789	11,672	23,019	20,022	46,214	51,594	2,001	2,269	52,878	46,715
Akron-----	574	857	79	121	140	166	308	530	33	40	211	171
Atlanta-----	1,812	2,642	456	654	567	906	880	1,062	20	20	796	627
Baltimore-----	7,822	9,091	843	612	747	648	1,514	1,035	47	46	1,868	2,597
Birmingham-----	3,193	4,549	225	423	876	1,298	780	1,159	55	120	397	672
Boston-----	1,204	1,359	235	200	0	147	774	884	30	47	884	805
Buffalo-----	1,346	1,240	157	106	161	21	995	1,065	33	48	592	657
Chicago-----	10,419	11,469	1,695	1,586	2,469	2,312	6,050	7,267	205	304	8,762	8,721
Cincinnati-----	2,036	2,388	271	264	(*)	(*)	1,765	(*)	(*)	(*)	662	690
Cleveland-----	2,731	2,556	502	430	887	593	1,278	1,451	64	82	1,018	999
Columbus-----	1,065	1,011	218	122	234	213	565	638	28	38	225	279
Dallas-----	1,699	2,252	318	282	345	351	1,023	1,598	12	20	492	795
Dayton-----	1,193	794	135	119	336	141	685	504	37	26	492	185
Denver-----	1,361	1,425	305	258	363	250	506	858	41	38	1,222	712
Detroit-----	7,988	5,635	1,028	765	2,434	1,416	4,384	3,330	142	124	3,878	3,332
Honolulu-----	346	467	45	181	43	59	229	203	29	24	758	774
Houston-----	1,291	2,944	209	219	460	1,064	586	1,571	36	90	1,512	743
Indianapolis-----	1,513	2,765	386	399	52	67	372	681	19	28	70	380
Jersey City-----	344	488	35	38	75	75	226	357	18	18	29	36
Kansas City-----	1,214	1,428	206	205	228	189	731	893	45	59	647	599
Los Angeles-----	7,387	5,147	0	90	2,923	1,731	4,251	3,184	213	142	3,355	2,993
Louisville-----	1,410	1,887	245	206	257	335	585	1,134	15	42	602	889
Memphis-----	4,584	5,257	395	451	2,152	1,802	1,971	2,835	66	69	3,661	1,767
Milwaukee-----	335	365	32	57	5	5	283	297	2	6	121	81
Minneapolis-----	462	583	72	61	80	100	298	414	10	14	530	466
Newark-----	1,523	1,729	190	237	400	446	884	1,014	49	32	595	728
New Orleans-----	1,855	2,298	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	1,383	704
New York-----	16,964	17,677	2,999	2,325	3,795	3,219	9,558	11,080	405	474	9,209	7,493
Oakland-----	1,012	855	120	97	247	204	605	512	30	22	927	607
Oklahoma City-----	1,306	1,234	133	182	351	396	408	401	32	18	648	520
Omaha-----	374	776	34	82	200	148	113	506	18	29	328	528
Philadelphia-----	6,648	2,205	226	(*)	716	(*)	(*)	(*)	52	(*)	599	(*)
Pittsburgh-----	6,177	5,445	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	88	176
Portland-----	578	503	164	96	34	33	370	348	10	27	721	429
Providence-----	343	366	52	20	31	27	226	289	6	10	111	99
Rochester-----	182	208	34	16	14	(*)	130	182	4	9	189	141
St. Louis-----	4,097	3,003	534	380	1,359	924	2,067	1,614	127	85	1,336	737
St. Paul-----	194	344	24	32	31	44	123	247	9	12	196	134
San Antonio-----	812	1,097	110	94	212	281	453	660	28	46	921	659
San Diego-----	777	685	70	75	225	218	422	382	27	9	607	451
San Francisco-----	1,971	2,395	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	1,427	2,195
Seattle-----	908	879	117	121	161	114	573	582	15	13	1,106	922
Syracuse-----	664	561	19	18	21	1	607	528	17	14	216	104
Toledo-----	640	449	97	48	118	78	401	299	24	24	86	118
Washington, D. C.-----	5,556	(*)	639	(*)	1,316	(*)	3,349	(*)	90	(*)	2,516	(*)
Actual total ‡-----	115,910	111,308	13,654	11,672	25,065	20,022	51,328	51,594	2,143	2,269	55,993	46,715

\* Data not available.

\*\* Includes "Not Stated."

† Based on cities reporting in both fiscal periods.

‡ Includes all reported cases.

<sup>1</sup> Based on 43 cities.

<sup>2</sup> Based on 39 cities.

<sup>3</sup> Based on 37 cities.

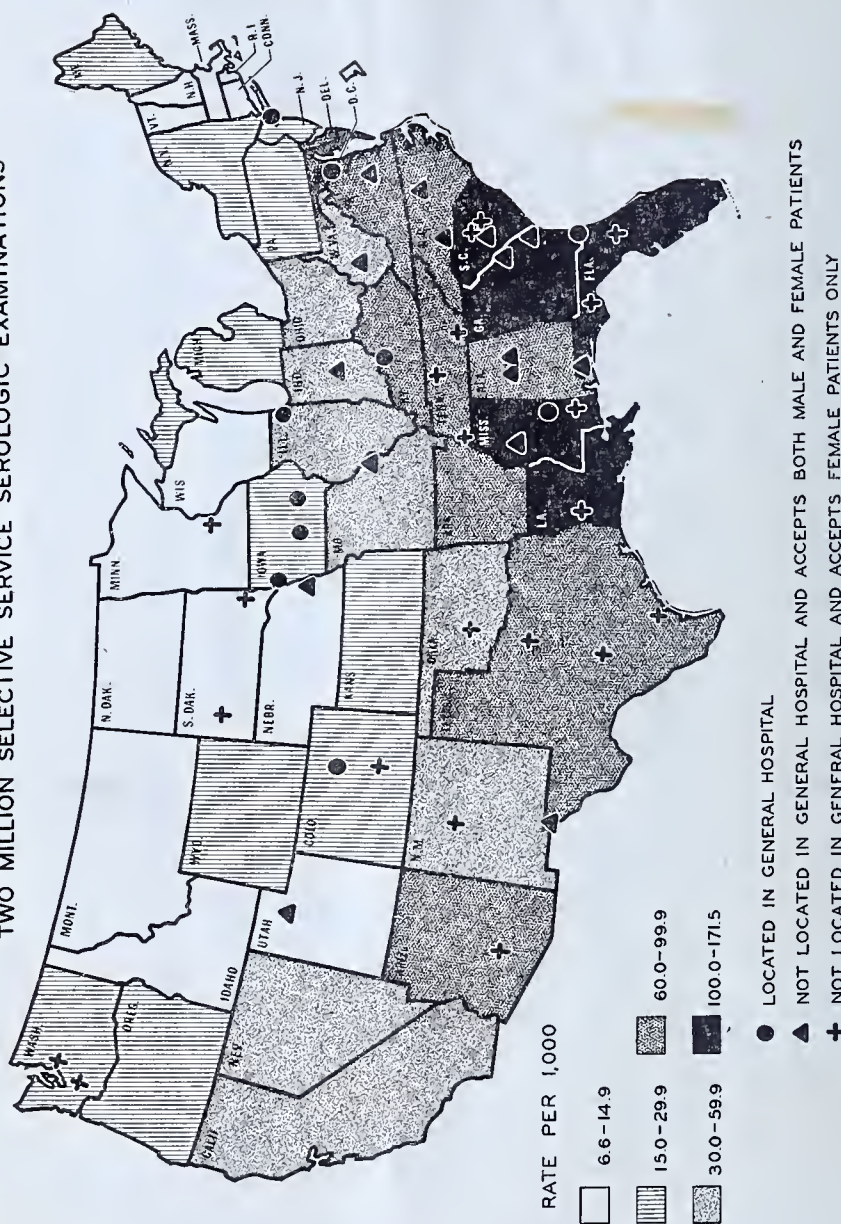
<sup>4</sup> Based on 38 cities.

<sup>5</sup> Based on 42 cities.

# VENEREAL DISEASE RAPID TREATMENT CENTERS ASSISTED BY LANHAM ACT FUNDS

(AS OF MAY 1944)

IN RELATION TO SYPHILIS RATES PER THOUSAND, DERIVED FROM  
TWO MILLION SELECTIVE SERVICE SEROLOGIC EXAMINATIONS





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FEDERAL SECURITY AGENCY  
UNITED STATES PUBLIC HEALTH SERVICE  
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# Some General Considerations Affecting Present-Day Sex and Sex Education Problems

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Allowing for the disposition of advancing years and war-time tension to make one see crises in everything, it would appear that a group of circumstances and influences are at work in the world to bring to a critical pass the human problem of sex. Not that there have not been peaks before, and that there will not be peaks hereafter; but this situation today is something of a third wave in an incoming tide, familiar enough to those who have watched beachfronts in nature, as in human affairs. Forming the crest and body of this wave one can recognize eight elements, all of them directly significant to a well-grounded basic effort to deal with the oncoming mass. These are summarized in brief topical dogmatic fashion in the following paragraphs.

## THE EMOTIONAL BACK-LASH OF MODERN CIVILIZATION

This might be framed in the question, "What has easier living done to the emotional tensions and tempo of mankind?" For a very sound physiologic reason well borne out in psychosomatic medicine, the disappearance from a civilization of the need for muscular effort as a means of neural tension discharge, leads inevitably to an overbalancing of the individual economy toward the emotional side. To bring this principle to the American scene, no ice to break on the pitcher in the morning; no chores; no 2-mile walk to school; no field to plough; no axe to wield—in their place, the running hot and cold water, the inner spring mattress, the soft car-seat, without even the necessity of twiddling a thumb to shift a gear,

the sit-down job, the over-sized meal—all such devices tend to create or to accumulate instead of draining off, the emotional potential of which sex forms so large a part. In the life of today, massive physical weariness obliterating all titillative stimuli from ankles to curvesome lips under a thick pall of muscular exhaustion, forms just no part at all. A rise in sexual tension and tempo would therefore seem inevitable. Nor does the upswing in the worry curve of modern life exert a necessarily compensatory depressant influence. In fact, one of the paradoxical things about worry is its direct drive into sexual hyperactivity and abnormal sexual practice. Sex activity is a major mechanism of escape. Another elementary critical reversal is that now developing between the role of man and of woman in the carrying of the physical load of life. Increasingly one sees the woman, liberated by marriage or a job from the time-honored but exhausting routine of washboard, iron, and kitchen sink, to say nothing of the children, pigs, and chickens, who has now become through accumulated and released emotional tensions, the sexual desirer, seeker and aggressor, of the male-female combination in the family life. The man comes home from a bad day, flat, to meet the woman, with her war-paint on, ready for the night-club and what have you. The result—adventurousness in sexual forms at an age and in social groups in which in the good old days sheer fatigue applied its damper, and the integrity of the home was assured, at least, of the stability of inertness and exhaustion.

## II. THE SEXUALIZATION OF CIVILIZATION

On this it is quite unnecessary to dilate to an audience of other than Rip van Winkles. One's chief concern in thinking about the sex coloring of modern life

This paper outlines the philosophy back of the organization and operation of a course in Health and Human Relations given last year by the Institute for the Control of Syphilis, Graduate School, University of Pennsylvania, Philadelphia, and to be repeated from June 26 to July 28, 1944.

must be not to forget his own youth, lest he substitute an endocrine atrophic viewpoint for a just psychologic and social appraisal. The thinning and disappearance of clothes, the ribaldries and near-pornographics of "cheese-cake," beauty parades and pin-up girls, the literature of erotic frankness, and the under-the-counter stuff which we have always had with us can be discussed pro and con, ad infinitum. Sex in the barnyard, in the school out-house, in the hay-mow, has been replaced by sex in the school club, sex in the all-night movie theater, sex on wheels, in the rooming-house, and in the bush. As a civilization takes on a more and more frankly sensuous nature, it is to be expected that the mode of dealing with the placement of sex in human conduct must undergo change.

### III. THE SHIFTING FRONT OF VENEREAL DISEASE CONTROL

A shift is impending, and indeed now in process, in the control front of the great public health problem of sex-disseminated and sex-associated disease. A riskless, quick, cheap, painless and near-infallible treatment for the punishment of sin, is now so close at hand that the venereal disease problem seems in many of its medical aspects at least, actually to be in the bag. That some of this anticipated beneficence may be wishful thinking will almost certainly prove to be the case; for quick and easy cure is turning out, as Pelouze has indicated for gonorrhea, to be less of a device for the control of infection than an incentive to epidemicity through incitement to exposure. Venereal disease dissemination takes place in the period between infection and the institution of treatment control. It is not the patient under treatment who spreads disease, but the promiscuous individual before and after treatment. The asymptomatic phase with protracted infectiousness induced by sulfonamides inadequately used or short of cure, in patients who have not been made simultaneously to appreciate the possibilities of infectious relapse and the necessity for prolonged patient observation and control is a current menace. Reducing the cost and discomfort and eradicating the danger of

treatment while assuring the cure of an increasingly high proportion of those who acquire venereal disease is not enough. One must reach forward somehow into the pre-treatment and post-treatment exposure fields. In other words, we must move against promiscuity rather than, in addition to, disease. Else the liberalization of sex practice which follows the conquest of venereal disease as such may compare with that which has followed contraceptive practice. If sexual relations lead neither to significant illness nor to unwanted parenthood, only a few intangibles of the spirit remain to guide the children of our science from an unmoded past into an unbridled future. We who cannot look upon this prospect with equanimity had best arouse ourselves. What better form could this arousal take than a revival of our social hygiene ideology, a return to first principles, long obscured by the control authority's stertorian call to treatment rather than prayer.

### IV. THE DISINHERITANCE OF THE HOME AND THE DECLINE OF THE FAMILY

This group of considerations might well have been placed first in the directorial group's thinking on the problem of how to get together a faculty and curriculum for a course in Health and Human Relations. It was in fact, the very first first thoughts as both faculty and curriculum will, perhaps, indicate. The family is the Rock of our salvation. The substitution of "mechanized" equipment and living techniques for the long-established energy-absorbing, energy-expending and energy-rewarding plans and equipment of the old-time home, around which the sex life of man has centered from time immemorial, has certainly not been an unmixed benefit. At today's one extreme the glossy model home, a deification of lighting, heating, interior decorating and the laborless household arts; at the other extreme, the two-room flop, with bathroom reinforced by the husband-and-wife-and-one-child-or-dog club sedan (or helicopter) has replaced the sometimes out-at-elbow living machine in which five- to eleven-child families in a generation or two reduced to rubble the structure and fu-



ishings that made men and women of them all. Nowadays there is no woodshed or the bucksaw and the tanning process; no chopping block to head off axe murders; no rain-barrel for our hollers, no cellar-door to slide down, and no apple-ree. The guinea-pig or white rat hatches its eggs under glass in the first grade classroom in lieu of the ancestral pig in the sty beside the barn. Every bathroom is a room attached, instead of every household one bathroom, and that divided between the laundry and the yard and the nearby orchard. When one considers that the common bathroom alone has one for sex and human education in the past, one wonders a little at the intrinsic virtue of privacy.

*The decline of duty.*—The prevailing hedonism of the day, the displacement of social or group standards and thinking by purely personal and individualistic action and thinking, provides a character problem in sex and self-control. So far as the life of the family is concerned, this shift in emphasis is a disintegrative force. Enforced escape from inadequate plant and equipment for self-expression by both group and individual; the scattering and the disappearance of the pull-together-for-the-group; a wandering at large in a forest of subversive influences without adequate guides for the individual, the younger one especially, has brought about the triumph of "I like" and "I want to" over "I ought to" and "I should." The decline of duty as a motivating force in human conduct is, then, one of the genuinely alarming moral trends of the day. Fortunately it is checked short of a runaway and smash-up for mankind at large by an inexorable survival mechanism in that nations and individuals who lose the cooperative and coordinative influence of a sense of duty to country, to home and family and friends, as well as to themselves, ultimately disintegrate. While the upswing of sex is on, it can be expected that its pleasures will be sought after with an unrestraint proportionate to the decline of the family which is at once sex privilege's institutional self-discipline and its reward.

*The rise of cynicism.*—Though at first glance it seems to stretch a point to associate it with the decline of the family, one cannot but be impressed by a trend towards cynicism, for which more than anything else, a robust and sound family life, with its full outlet for idealisms, and its adequate physical and psychological controls of resentment serves as antidote. The wise-cracker and the superficial sophisticate thrives in shallow surroundings which, regardless of their physical surface range expressed in speedometer miles, lack the depth and perspective-giving qualities of the family that is grounded on the land.

#### V. THE DISAPPEARANCE OF JUVENILITY

Have you noticed the rate at which children grow up nowadays? To one who sees the dermatology of childhood and youth, the telescoping of adolescence by oncoming adulthood is a constant source of astonishment. Something must be happening to the pituitary, to say nothing of the gonads these days, and pubescence seems to be moving down the physical line towards childhood, making the thirteen-year-old-girl the equivalent in physical sex maturity of the young woman five years or more older a generation or so ago. When one looks at these child-men and child-women—more especially the latter—and then talks with them fundamentally enough to take some soundings on their minds, he finds that there have been thrust forward upon the immature and unstabilized years of life a physical equipment and an urge for which there is no compensating intellectual and experiential equipment to guard the vital decisions that their precocious sex equipment thrusts upon them. There is perhaps in some layers of the social upper tenth a compensating tendency to greater general intellectual maturity at birth. Side by side with the eczema-asthma-hay-fever complex, the childhood of the most developed part of the community intellectually is showing preformed maturity of mental structure. Children are born with whole blocks of intellectual equipment, with behavior patterns these days evident in the first few months of

life that have anything but the soft amorphous powder-puff quality of infantile mentality which family and school educational practice and theory had developed as the "molding" concepts of child psychology of thirty-five years ago. Perhaps oncoming intellectual adulthood will overtake sexual precocity and protect the adolescent (if such there be) from the consequences of emotional decisions made by his endocrines and his thalamus before his cortex and association centers awake to the reasoned requirements of his all around welfare. The educational process can perhaps assist, earlier and earlier in life, in the identification and utilization, as well as control, of strongly marked behavior trends and patterns in the precocious child, in advance of puberty and awakened sex consciousness. Evidently the developmental processes of the child, the ontogeny and phylogeny, are of first importance in a course in Health and Human Relations.

#### VI. THE FADING OF THE AUTHORITARIAN TRADITION

Bossard, in his "Family Situations," has drawn a particularly fine word picture of what he calls "the democratic family." A sharing of views on family and personal conduct and decisions as to that conduct in a species of forum among all the members of the unit social group is something devoutly to be wished, but in its general attainment is still far in the future. We are likely to see a number of swings before the indicator hand of teaching emphasis comes to rest somewhere between adult and child dominance. At the moment, youth talks up to age, rather than age down to youth. There is an obvious decline in the rating of experiential guides and maxims quite understandable when one examines the afore-described endocrine background of youth and the age level and resultant endocrine status of sage advice in general. As a sign of authoritarian decline, consider the disappearance of mottoes from the kitchen wall and that incredible loss to the structural framework of social character, the vanished Spencerian copy-book which was for our day a modern version of Aesop's Fables, whose wise

saws have done so much to epitomize laudable conduct from the past, for the present and future. "God bless our home" has vanished, along with "Honesty is the best policy"; "Practice makes the master"; "A penny saved is a penny earned"; "A stitch in time saves nine." Many another precious increment of knowledge and character guide-post, none of them particularly sexy in flavor but all part of the structural steel of character equipment, which is, after all, the structural steel of the sound sexual life, has passed into the attic if not the discard. It will be inevitable, and indeed desirable, that the fading of the authoritarian tradition be frankly accepted, and youth be drawn as a coequal, into the councils of the elders in the sexual mores and solutions of the future.

#### VII. A TURNING TO SUBSTITUTES

"Passing the buck" is our most human failing, and it reached one of its peaks in Machiavellian ingenuity when we began handing over to other mechanisms like the school, the educational functions of the delinquent and deteriorating home. The school system is at the receiving end of a colossal buck-passery these days, and has to do everything in the name of home, family, intellectual and emotional development, and even sometimes God, that the trouble-evading and ingenious not to say lazy human being and his once familial aggregations can push off onto it. The job of functioning as a substitute is, in itself, discouraging and difficult. But the disposition on the part of the schools to accept the delegated responsibility without protest and the most critical self-examination, would be a deeper cause for anxiety.

#### VIII. THE JOINT-LOOSENING EFFECTS OF WAR

Instead of a long discussion of what must be obvious to the audience to which this summary is addressed, a short three words on the effect of war from the considered appraisal by an officer in the armed forces who in close contact with the rank and file, has neither a puritanical nor a laissez faire viewpoint toward the conduct of human life, will answer: "War makes bums." A certain amount



of separating of sheep from goats by war is to be expected. It is to be hoped that before the struggle is over, there will have been injected into it what it seems thus far to have lacked for us—a selfless and idealistic dedication to a human ideal; else we shall come out of it with our disproportionate share of goats. Never in the range of human experience have we more desperately needed a dedication to a forward-looking and unselfish ideal than in the sex life of man at this moment. In no way could we suffer a worse loss by the long-range deteriorative influences which mark the spiritual exhaustion of a long war.

Like education in general, sex education had accepted and is now swinging away from or wearing out the authoritarian tradition. It has been from above downward—parent to child, pastor-to-flock, God-to-man stuff, in which the recipient had better conceal his doubts, rebellions, and resentment, or else—. Reading the April issue of *Harpers*, I met exactly the words I wanted for this particular paragraph, in Vivian Thayer's discussion of Religion and the Public Schools. They give new force to the principle that preceptor and pupil are one, and on a common level in that both must live the life they teach and are taught:

"Character, moral behavior, grows out of a way of life which people not only profess in common but practice in common; and where profession is sincere, it is the practice rather than its conscious formulation that is primary in educational growth. Accordingly, if we are genuinely concerned that our children shall acquire habits and ideals of honesty, fair play, self-control, generosity, and respect for the personalities of others, we will have to create conditions of living in home and school and community that embody these ways of acting, feeling, and thinking. In short, moral ideals, as moral practices, evolve out of the culture in which men participate. They are rooted in the common and approved ways in which people deal with one another."

In the light of such a statement, what can we do other than to repeat the words of the Episcopal Collect—"We have left undone those things which we ought to have done, and we have done those things which we ought not to have done." The children and the youngsters of today re-

produce more than anything else their parents and their parents' friends. In the words of the good old Spencerian copy-book and Aesop's Fable, "Example is better than precept"; and no better example could be found of a break between precept and example than the sex and family conduct of today.

Let us concede that sex education as it has been taught, or rather, preached, has had a certain hypogonad quality. Coming from above downward, from the sage to the ignorant; from age to youth; it would be inevitable in medical terms that a certain amount of dehydration—juicelessness—would have crept into the format; that there would be less testosterone and progesterone, more calcification and fibrosis, less heat, even though more of a colder light. It sticks out all over many of our plans and proposals as one reads of them, that as reduced to black and white, they simply will not go over with the daughters and sons, whose rounding curves and broadening shoulders and bulging thews and sinews evidence their sexually built-up and precocious youth. Somehow the children must be able to feel that we advise as we do, not because we have cooled off or never warmed up, but because we are warm, *hot* ourselves, and know that fire burns, and let loose, destroys.

There attaches to sex education—and it is a fertile source of cynicism particularly among physicians with regard to educational efforts—a certain fog of vagueness, a quality of no-point, no vernacular, little realism, much pious wish and wishful thinking at the 'age level of the thinker. The extreme of revolt against this evident deficiency in educational mechanism and technic is, of course, the barroom and night-club approach of the recent Detroit demonstration. The educational ideal must be an earlier approach in franker vein to the everyday facts. What can and do John and Mary learn in the bathroom? Nothing is worse needed in health and human relations than the development of an adequate vocabulary and the power, given to too few, to swing it.

An educational program must rest upon a *scientifically examined and sound fac-*

tual basis. It must be apparent that here the educational agency is suffering under a grave handicap. Fact and theory appear to be two different things—closed compartments thus far with contents immiscible with and inaccessible to each other. The prunes at the intellectual breakfast table of the schoolma'am, and the beer and garlic of the realist's diet must somehow be brought together. A large part of the literature is opinionative, like this paper. Factual material critically examined, like Catherine Ben-sent Davis's study of the sex lives of a large group of women at the collegiate level, and perhaps Kinsey's present well-directed inquiries, are landmarks, or shall we in nautical phraseology, say spindles indicating dangerous sunken reefs in the sea of thought. Much effort must be directed in the next few years at a precise delineation of the individual human sexual solution, for sooner or later every human being who does not achieve suicide, and indeed some who do, achieves some kind of sexual solution. We are proceeding on a wholly arbitrary group of value-conceptions, ranging from the extreme of uninhibited self-expression to the pseudo-asceticism of the hypogonad types. Somewhere before we begin to do very serious teaching, by a process of inquiry and conference, must be found a formula or a group of formulas for the intelligent sexual life.

The delegatory buck-passing of sex education onto the school system forces from us the admission that the school system itself needs and in the past has not perhaps fully received appraisal and evaluation of itself as an instrument and agency in this field. It has been more than once suggested that teaching, itself defined by Henry Plummer as "an hereditary neurosis," is by no means the human occupational instrument nor are teachers as such the types through which so emotional and unbalanced an affair as average sex conduct should be determined, mediated or "instructed." There must be prompt and diligent inquiry as to the fitness of the school system and its personnel for the undertaking in hand and the first instructional effort must be expended upon

the educator, rather than on the educatee.

In the educational effort of the past, there seems to have been a notably undemocratic, non-conference type of approach. There have been conferences to be sure, but too often merely conferences at the big-wig or the teacher or the professional level. Conferences drawing on the ordinarily voiceless family, the potent but also voiceless neighborhood, the various age levels in the sex problem—especially self-governing or gang-active youth—seem to have been few indeed. The ball for our present course in Health and Human Relations was started rolling by a conference between public health and educational agencies that certainly is none too common. If the course is to be taught along broad effective lines, one of its deepest roots must tap a mechanism and equipment for *health education*. A conference approach must then be had which will tax the ingenuities and the acquaintance range of those who undertake it to the utmost, and every care must be taken to see that the ball is *not* passed to a tight group which either has all the answers, or announces with equal force that there is no answer.

There has been in the educational effort of the past in the field of sex, a disposition to *mass handling* of what can never be a completely rubricated general-solution, aggregate-handled problem. If there is any one thing that stands out by implication from the field of venereal disease control, it is that sex problems, like the control of the diseases that spring from them, are local, distinctively local, affairs, taking on their color, form and foliage from the soil from which they immediately spring, and as closely conditioned in their management by their social, psychologic, economic and physical origins as the lives of plants and pathogenic organisms. Such a statement is not intended to exclude the worth of general principles in the study and determination of solutions, but it does emphasize the fact that the point of application of principles will be local and their effectiveness determined within very narrow limits by place, time and individual con-



ditions. In a school system, this becomes a matter of the utmost importance. Solutions and principles that work in school A in system X, may not work in school B in system X, to say nothing of school C in system Y. It would be preferable, therefore, in organizing a conference approach to a problem in health and human relations, to pay at least as much atten-

tion to the definition and management of individual problems and the selection of persons to undertake them as to the development of instructional programs at large. That perhaps is one of the reasons why the paper solution and the committee resolutions so often have that fogged quality and that pious wishful ring. They don't get down to brass tacks.

## **Epidemiologic and Clinical Study of Sulfonamide Resistant Gonorrhea: Report of Three Cases**

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The diagnosis, treatment and epidemiology of gonorrhea is very important in the wartime control of increased incidence of venereal diseases. It is well recognized that the problem is more difficult and complex in the female than in the male (1, 2). That the sulfonamides are not the panacea for cure of gonorrhea is realized (2, 3), and the need for careful test of cure is necessary in not only the female but also the male. As Cox (4) has pointed out, the tendency to self treatment is a public health menace, because the patient assumes that the disappearance of symptoms means a cure, and thus some patients may become symptom-free carriers. During the past year it has been noted in our clinic that an increasing number of gonorrhea patients have appeared to be resistant to sulfonamides (5, 6, 7). The use of penicillin in sulfonamide resistant gonorrhea has been reported as successful in such cases (8, 9, 10). The present report is made because of the interesting clinical observations of resistance to sulfonamide therapy and the apparent epidemiologic relationship in three young girls who possibly were infected with the same strain of gonorrhea.

The cases which are presented all reported that they had had sexual intercourse with Case 1 G. K. (43-1539-1), a white, single male, age 18. These sexual contacts were reported to have occurred on the same night, July 20, 1943 and two of the girls had had previous contacts with

him within a few weeks. Although we were never able to bring the patient (G. K.) into our clinic for examination, due to the fact that he was a member of the Merchant Marine and out of our jurisdiction, it was confirmed that he had been treated at a station hospital with sulfonamide therapy (type ?) and protargol, 1/4 percent solution instillations, for acute gonococcic anterior urethritis, proved bacteriologically. According to the report, he was discharged on June 14, 1943 after three negative urethral spreads. No mention was made as to whether the infection was resistant, and no contact information was given. Through investigation it was found that this patient had been treated for gonorrhea about one year previously, and that he had obtained a sulfonamide (sulfathiazole) prescription in the spring of 1943, apparently for self treatment as needed.

Case 2 B. B. (41-383-12), a white, single female, age 15, was the first of these patients to come to the clinic (Aug. 6, 1943), with symptoms and signs suggestive of acute gonorrhea of approximately 2 months' duration. She had had sexual intercourse with G. K. on three occasions during June and July 1943. He had given her sulfathiazole tablets, and she had taken 2 tablets three times a day for 2 days before coming to the clinic. There was no previous history of gonorrhea or other previous sulfonamide therapy. Spreads and/or cultures were positive for

gram-negative intracellular diplococci resembling *Neisseria gonorrhoeae* on Aug. 6 and 9, Sept. 30, Oct. 6 and 27, and Nov. 3, 1943. Sulfonamide therapy was given as follows: On Aug. 6 sulfathiazole 1 gm. four times daily for 7 days; Sept. 13, 0.5 gm. sulfathiazole four times daily for 14 days; Oct. 6, sulfadiazine 1 gm. four times daily for 7 days; Nov. 3, sulfathiazole 1 gm. four times daily for 7 days. There were no clinical signs of toxicity, and rechecked blood counts and urines showed no evidence of toxicity. With the last course of sulfathiazole, bed rest was insisted upon for 1 week, and when last seen on Nov. 10 and 15 there were no clinical signs of discharge, and spreads and cultures were negative.

The patient then moved to northern California, where, through the cooperation of the Yolo County Health Department at Woodland, she was observed periodically from Nov. 30, 1943 through Feb. 10, 1944, during which time she had 5 spreads and cultures, which were reported as negative. She received no further sulfonamides after Nov. 3, 1943. *Trichomonas vaginalis* was found during observation at our clinic and at the Yolo County Health Department. No local treatment was used for either the gonorrhea or the trichomoniasis except occasional low pressure douches and Sitz baths. When last seen, the patient was clinically well.

Case 3 P. B. (43-1076-4), a white, single female, age 16, was referred on Aug. 9, 1943 by Case 2 because of signs and symptoms suggestive of acute gonorrhea of about 1½ months' duration. She had had three sexual exposures to the same reported "source" during June and July 1943. She had also taken 6 sulfathiazole tablets given her by G. K. about 1 week before reporting to the clinic. There was no history of previous gonorrhea or other sulfonamide therapy. Her last menstrual period was early in August 1943 and she was later found to be pregnant. Physical examinations revealed signs suggesting acute gonorrhea. Spreads and/or cultures were positive for gram-negative intracellular diplococci resembling *Neisseria gonorrhoeae* from urethra, vagina, and/or cervix on Aug.

9, Sept. 8 and 15, Oct. 6 and 25, Nov. 8, Dec. 6 and 11. She received sulfonamide therapy as follows: On Aug. 9 sulfathiazole 1 gm. four times daily for 6 days; Sept. 15, sulfathiazole 1 gm. four times daily for 7 days; Oct. 25, sulfadiazine 1 gm. four times daily for 7 days (these she took in 11 days because some of the dosage was taken three times daily). There was no clinical evidence of toxicity, and rechecked blood counts and urinalyses were negative. *Trichomonas vaginalis* was an incidental finding, and there was considerable whitish gray vaginal and cervical discharge when patient was last seen.

Because of the persistent bacteriologic evidence of gonorrhea, she was referred to the Los Angeles County General Hospital for penicillin. While there she received 17 gm. of sulfathiazole (1 gm. four times daily) between Nov. 27 and Dec. 1. Positive cultures (urethral-cervical) were obtained on Dec. 6 and 11. Penicillin, 25,000 units every 4 hours for 5 doses, was given intramuscularly (gluteal) on Jan. 1, 1944. Following this she had 6 negative spreads and cultures between Jan. 5 and 10. Since then she has been followed in the Ruth Home, an institution for venereally infected, unmarried pregnant girls; she had 4 negative cultures and spreads between Jan. 26 and Feb. 23, and the physical examination is reported as negative.

Case 4 L. S. (43-1525-2), a white, single female, age 15, was referred on Aug. 9, 1943 by Case 2 because of signs and symptoms suggestive of acute gonorrhea of approximately 3 weeks' duration. She had had no menstrual period since June 1943. There was no history of previous gonorrhea nor of previous sulfonamide therapy. Physical examination revealed signs of acute gonorrheal urethritis, vaginitis and cervicitis, and condyloma acuminatum lesions were seen around the vulva. Spreads and/or cultures were positive for gram-negative intracellular diplococci resembling *Neisseria gonorrhoeae* on Aug. 9, 13 and 23, Sept. 11 and 15, Oct. 4, Nov. 17, Dec. 2, 1943 and Jan. 1, 1944. Sulfonamide therapy was given as follows: On Aug. 9 sulfathiazole 1 gm. four times daily for 7 days; Sept. 1, sulfa-



thiazole 1 gm. four times daily for 6½ days; Sept. 15, sulfadiazine 1 gm. four times daily for 5 days; Sept. 27, sulfathiazole 1 gm. four times daily for 7 days; Oct. 14, sulfadiazine 1 gm. four times daily. (She had taken 11 gm. before she was sent to Ruth Home.) At Ruth Home sulfathiazole 1 gm. four times daily between Oct. 19 and 23, and sulfadiazine 1 gm. four times daily between Oct. 23 and Nov. 10 was given with semi-bed rest. Only one spread was taken there, and this showed only pus cells.

On Nov. 22 she was sent to the Los Angeles County General Hospital where a spontaneous miscarriage of a six-month-old fetus occurred. While in the hospital she received 6 gm. of sulfadiazine Nov. 24 and Nov. 25; typhoid vaccine, 50 million killed organisms per cubic centimeter intravenously on Dec. 7; 75 million on Dec. 20 and 100 million on Dec. 22 with a total of 5 hours of fever 103° F. or over. Positive cultures were obtained on Dec. 2, 1943 and Jan. 1, 1944. Recommendation was made for penicillin, and on Feb. 3 she was given 25,000 units intramuscularly every 4 hours for 5 doses. From Jan. 20 through Feb. 12 while in the hospital, 7 consecutive negative spreads and cultures were obtained. A gynecologic consultant remarked that creamy discharge from Skene's glands persisted in spite of 6 negative spreads and cultures. This case is now being followed in our clinic and the same discharge has persisted up to the present time. No further therapy for gonorrhea has been given. Spreads and cultures were negative on Feb. 23, Mar. 17, and Mar. 29. *Trichomonas vaginalis* was an incidental finding in this case also. No local treatment was used in this case except occasional low pressure vinegar douches and one series of vaginal suppositories for the trichomonads. There was no apparent toxicity from the sulfonamides or other treatment, clinically, by blood counts, or by urinalyses.

Repeated blood serologic tests for syphilis have been negative in all three girls. All stated that they took the sulfonamides that had been proffered to them by G. K., and we assume this was true since the girls seemed cooperative

and anxious to overcome their infections. We do not believe that reinfection was a factor in these cases. However, one of the girls, P. B., did admit sexual contact once in October 1943, after coming to the clinic. The "contact" was examined and found to be negative for gonorrheal infection.

#### COMMENT

Although we have not been able to prove that these three girls acquired their infection from G. K. (Case 1), we do know that he had an acute gonorrheal infection and that all three girls had sexual contact with him on one or several occasions shortly after he was discharged as "cured." The question arises whether he was actually "cured," or whether he was an asymptomatic carrier with a resistant organism. We know that he did have in his possession sulfathiazole tablets and had given them to two of the girls after his contacts with them. Self-treatment of gonorrhea may lead to the development of asymptomatic carriers and the perpetuation of sulfonamide resistant strains of *Neisseria gonorrhoeae*. It is probable that, with the discharge in military and civilian practice of cases of gonorrhea without adequate tests of cure, a certain number of the men will become asymptomatic carriers (2, 3, 4).

We may contend that the strain of *Neisseria gonorrhoeae* with which these girls were infected was the same sulfonamide resistant strain, although one girl (Case 2) did apparently respond to sulfonamide therapy. (Or possibly she had a spontaneous "cure"?) The infection in all three girls was definitely an acute clinical gonorrhea when first seen. Abundant gram-negative intracellular diplococci resembling *Neisseria gonorrhoeae* were repeatedly found in spreads and cultures in urethral, vaginal and cervical specimens. No complicating condition of gonorrhea was present in any of the cases, except that L. S. now has a bacteriologically negative skenitis. Douglas and co-workers (11) reported that in their series of cases the duration of the disease, site of the infection or factor of pregnancy did not affect the efficacy of treatment with the sulfonamides. It would have

been of value and interest to have bacteriologically proved that the infecting organisms were resistant to sulfonamides. By a method such as reported by Goodale and coworkers (6) valuable time and effort may be saved by showing that the organisms are resistant to the drug and directing the therapy along other channels. However, this was not possible in these cases and evidence must be based on clinical and epidemiologic findings.

The factor of pregnancy in two of the cases raises the question as to whether this caused any change in response to the sulfonamides. However, other reports have shown that infected pregnant women respond as well as nonpregnant women (11, 12). Case 2, who had not been pregnant, had the only "cure" without the use of penicillin. This patient also followed the suggestion of bed rest better than the other two girls.

Penicillin was finally the method of treatment which made an apparent bacteriologic cure in Case 3 and Case 4. However, the latter patient still has clinical evidence of purulent urethral discharge (skentitis), although it has been negative by spread and culture in more than 8 tests over a two-month period. Strauss and Grunstein (13) have reported persisting discharge, although negative for gonorrhea, after sulfonamide therapy. One girl, P. B., was pregnant when given penicillin and the other, L. S., had a miscarriage spontaneously about 2 months before penicillin was given. She had also failed to respond to typhoid vaccine fever therapy. Although penicillin appears to be valuable in sulfonamide resistant gonorrhea (8, 9, 10), a large number of cases must be studied over a long period of time before a final evaluation can be made. Bacteriologic failures following penicillin have been seen in the female isolation unit at the Los Angeles County General Hospital.

This study also emphasized the need for investigation of the social factors concerned in the juvenile delinquency and the lowering of sexual morality which have been noted in wartime (14, 15). For here were three young, unmarried high school girls infected with gonorrhea, with two of them pregnant; because of need for prolonged medical treatment and

social readjustments, their normal family and educational relationships were totally disrupted. The solution of such problems should be the concern of educators, sociologists, physicians, and other community leaders.

#### CONCLUSIONS

1. Three cases of gonorrheally infected females are presented as clinical evidence of sulfonamide resistance, the infection probably being with the same sulfa-resistant strain of *Neisseria gonorrhoeae*.

2. Penicillin therapy was finally used in two of the cases and was apparently successful in obtaining a bacteriologic cure.

3. It is felt that an adequate follow-up and test for cure should be given in all gonorrheal infections, male and female, because of possibility of detecting asymptomatic carriers, for these may be a significant factor in the transmission of the disease.

4. It has been observed in our clinics that increasing numbers of patients have come for treatment who are apparently resistant to sulfonamide therapy. Many of these ambulatory patients, especially females, present difficult therapeutic problems in view of the great scarcity of penicillin and lack of facilities for fever therapy.

5. Factors contributing to increasing juvenile delinquency and lowering of sexual morals in wartime deserve the attention of community leaders.

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## Methods of Transporting Gonococci to Laboratories for Cultural Studies

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In a previous report on delayed planting of gonococcus cultures,<sup>1</sup> it was stated: " \* \* \* in the strength of 1:30,000 gentian violet inhibited the growth of many organisms but allowed the gonococcus to remain viable for long periods of time." This statement was erroneous. At that time we were using a supposed 1:100 aqueous dilution of gentian violet for the stock solution, small amounts of which were at various times further diluted with water to make a supposed 1:15,000 dilution. This latter dilution was mixed with equal parts of blood to give what was considered a final dilution of 1:30,000. The insolubility of gentian violet in water was not then appreciated. During the past year we have used a 1:1,000 alcoholic solution, a sufficient amount of which is added to the other ingredients to make a final dilution of 1:800,000 to 1:1,000,000. Experiments have shown that these dilutions do not seriously inhibit the growth of gonococci but that more concentrated dilutions do. It is our opinion that in our earlier experiments the gentian violet was, in fact, in

much greater dilution than was thought to be the case. During the past year, also, we have used horse serum in place of defibrinated horse blood. To the horse serum is added a sufficient amount of 1:1,000 alcoholic dilution of gentian violet to make a final dilution of 1:800,000.

Although gonococci can be kept viable for as long as 48 hours and subsequently be successfully cultured, the method which we have described has too often proved to be inefficient. In an attempt to explain the failures, a series of 24-hour viability tests were run on serums from 36 different horses. Twenty-one of the horses had been used for immune serums: 6 for diphtheria, 1 for scarlet fever, 3 for meningitis, 6 for pneumonia, 1 for diphtheria and influenza, 1 for diphtheria and meningitis, 3 for diphtheria and pneumonia. Fifteen were so-called normal, i. e., they had not been used for immune serums.

Gonococci from pure cultures of recent strains were transferred on swabs to tubes containing the serums. The tubes were identified and were then kept at room temperature for 24 hours, following which the swabs were streaked onto starch agar plates which were incubated for 48 hours at 36° C. in candle jars.

<sup>1</sup> Cox, O. F.; McDermott, M.; Mueller, J. H.: Delayed planting of gonococcus cultures: Preliminary report. *Ven. Dis. Inform.*, 23: 226-27, 1942.

Plates planted with material that had been in the serums from the different horses gave the following results: The diphtheria horses, good growth in 5 and poor growth in 1; the scarlet fever horse, no growth; the meningitis horse, no growth; the pneumonia horses, no growth in 4 and poor growth in 2; the diphtheria and influenza horse, no growth; the diphtheria and meningitis horse, no growth; the diphtheria and pneumonia horse, no growth; the 15 normal horses, good growth in 10, fair growth in 4, and poor growth in 1. These experiments suggest that serums from horses that have been immunized with the meningococcus or the pneumococcus are not suitable for maintaining the viability of the gonococcus.

To determine the length of time horse serum could be kept at room and icebox temperatures before it would subsequently fail to maintain the viability of gonococci the following procedure was carried out: A series of tubes containing normal horse serum which had previously been tested and found to keep gonococci viable were put in the icebox and an equal number were left at room temperature. The tubes were inoculated with gonococci at regular intervals and were kept at room temperature 24 hours before the specimens were planted. No growth was obtained from the tubes that had been kept at room temperature longer than 13 days, whereas good growth was obtained from the tubes that had been kept in the icebox for 3 months before inoculation. The experiment was not continued beyond 3 months.

An attempt was made to determine why serum left at room temperature for several weeks failed to keep gonococci viable. Rapid coagulation was tried in an effort to stop slow enzyme action. Fifteen tubes of coagulated serum were inoculated with gonococci. Attempts to recover the organisms after 24 hours were not successful in 14 instances and successful in 1.

Horse serum was then dialyzed, one batch in water and another in 0.5 percent sodium chloride. The beakers containing serum and dialyzing reagents were kept in the refrigerator 3 days and the dialyzates were changed daily. The serum in 0.5 percent saline remained clear without precipitate. The serum dialyzed in water

threw down the typical heavy white precipitate. The serum was divided into 3 lots: Lot 1, the serum dialyzed in saline, was transferred to small tubes using 0.25 cc. per tube; lot 2 was part of the clear supernatant serum dialyzed in water; lot 3 was the supernatant serum with the precipitate of the serum in water resuspended. Each lot was inoculated with a 24-hour pure culture of gonococci and allowed to stand at room temperature 24, 48 and 72 hours. Viable gonococci were not recovered from lot 3 but were recovered from lots 1 and 2 at 48 hours, although not at 72 hours.

A parallel series of tests was carried out as follows: Tubes containing serum from defibrinated blood, Seitz filtered serum, and serum from clotted blood, were kept at room temperature, and tubes from each set were inoculated on the fourth day and each succeeding day. Neither the serum from defibrinated blood nor the Seitz filtered serum was efficient after 6 days, and the serum from the clotted blood stood up well for only 11 days.

Previous experiments in which we attempted to cultivate gonococci from urines that had been mixed with equal parts of serum and kept at room temperature for 24 hours have all failed. However, when gentian violet was added to the serum the results have been more encouraging. We have recently carried out the following experiments: Urines from male patients were collected in sterile bottles and 1.5 cc. of each specimen was pipetted into three different vials: one containing an equal amount of 1:800,000 gentian violet in horse serum; the second, 1:2,000,000 Nile blue A in serum; the third, 1:35,000 tyrothricin in serum. The vials were corked and kept at room temperature for 24 hours, at which time they were centrifuged and the supernate discarded. The sediments were then streaked onto plates which were incubated for 48 hours. Ninety consecutive positive specimens were similarly tested. Gonococci were not detected in 27 of the gentian violet specimens, 24 of the Nile blue A, and 18 of the tyrothricin specimens. Of the 27 gentian violet negatives, 13 were positive in Nile blue A and 18 positive in tyrothricin. Of the 24 Nile blue A negatives, 10 were



positive in thyrothricin and 9 in gentian violet, and of the 18 thyrothricin negatives, 8 were positive in gentian violet and 4 in Nile blue A. All three were negative in 7 cases (controls positive). Four gentian violet specimens were positive when the other 2 were negative, as were 1 of the Nile blue A and 6 of the thyrothricin specimens. Gentian violet was 70 percent efficient, Nile blue A 73 percent, and thyrothricin 80 percent, and collectively they were 92 percent efficient. We now propose to conduct similar experiments substituting swab specimens for urine and, if it is shown that by using all three methods the percentage of positives is materially increased, that routine could easily be adopted.

#### CONCLUSIONS

A completely dependable method of transporting gonococci to the laboratories for cultural study is not yet available. The horse serum and dye method has, in our laboratory, proved less efficient than routine cultures but more efficient than the examination of stained spreads, particularly in women.

If horse serum is used its efficiency in maintaining viability should first be determined. Serums from horses that have been used for meningococcus- or pneumococcus-immune serum are probably not efficient.

Search should continue for a better method of inhibiting the growth of contaminating bacteria.

A previously described method for maintaining the viability of gonococci is recommended with certain modifications if routine culture facilities are not available.

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## DIAGNOSIS

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The Kansas evaluation studies of the performance of serologic tests for syphilis. Charles A. Hunter and Frank Victor. (Unpublished manuscript.)

In the fall of 1939, the Kansas State Board of Health approved the intrastate evaluation study of the performance of serologic tests for syphilis and appointed

a committee to assist the Director of Laboratories in the selection of donors, and in arranging other details regarding the study. A form letter was sent to all hospitals, institutions, and private laboratories explaining the purpose of the study and requesting that all laboratories desiring to enter this study make application. Replies from 26 laboratories indicated that they wished to participate in the evaluation study. Since this number was too large to handle efficiently, the 13 laboratories which did the largest volume of work were chosen. Of the laboratories participating in the 1940 study, 4 were evaluated on complement fixation tests, 6 on complement fixation and Kahn tests, 2 on complement fixation and Kline tests, and 1 on Kahn and Kline tests.

Arrangements were made to obtain half of the specimens from the necessary 225 donors from the Kansas City Health Department and the other half from the Sedgwick County Health Department, Wichita. The Venereal Disease Research Laboratory of the U. S. Public Health Service agreed to run the Kolmer, Kahn standard precipitation and the Kline diagnostic tests on these blood specimens, as a check on the State laboratory which was to serve as the control. Donors were to receive \$2.00 for the 75 cc. of blood which would be necessary for each specimen.

A second intrastate study was carried out in the spring of 1941. Twelve laboratories were chosen from the 31 which had expressed a desire to be tested. Donors were paid \$4.00 for 150 cc. of blood, and the physicians who took the clinical histories and assisted in collecting the specimens were paid \$2.00 per donor.

The results of these studies are shown in graphs. In the 1940 study, 6 of the 12 entrant laboratories in the complement fixation tests failed in both sensitivity and specificity, 4 in sensitivity, and 2 in specificity. On the Kahn test, out of 7 participating laboratories, 1 failed in both sensitivity and specificity, 5 were low in sensitivity, and none of these were below standard in specificity. On the Kline diagnostic test, all 3 laboratories entered were low in specificity and 2 were low in sensitivity.

In the 1941 study, of the 20 laboratories entered in the complement fixation tests, 3 were low in sensitivity, 6 in specificity, and 11 were satisfactory. Of the 25 doing the Kahn test, 1 was low in both sensitivity and specificity, 6 in specificity, 9 in sensitivity, and 9 met the standards required. All 6 laboratories entered on the Kline diagnostic test failed to meet specificity standards.

A comparison made of the results of the tests made by each laboratory in 1940 with those of the 1941 study shows a general improvement in their work. A number of serologists have taken advantage of the offer of the Division of Public Health Laboratories, Kansas State Board of Health, to act as a training school. It is planned to continue these evaluation studies in Kansas by working with the laboratories, offering them advice, consultation, training facilities and, at a nominal cost, standardized antigens.

**Mazzini test chosen by Army for rehabilitation program.** Monthly Bull., Indiana State Bd. of Health, Indianapolis, 47: 28, Feb. 1944.

The Indiana State Board of Health has recently been notified that the Mazzini test for syphilis has been chosen by the Army as the routine serologic procedure for the entire rehabilitation program which is used in the conquered areas.

Mr. L. Y. Mazzini, who is a native of Lima, Peru, began his work as a serologist on the staff of Indiana University School of Medicine about 20 years ago. In 1933 he was transferred to the State Board of Health to work in conjunction with the University and the State Board of Health. He is Chief Serologist at the Board of Health and Assistant Professor of Clinical Pathology in the University.

The Mazzini test has been patented and has been assigned to the Indiana University Foundation. It is the result of about 15 years of work in research and careful check testing. It is said to be one of the most sensitive and accurate tests for syphilis known to science on the basis of its official performance.

**Metastatic granuloma venereum: Report of a case.** L. C. Paggi and Edgar Hull. Ann. Int. Med., Lancaster, 20: 686-695, Apr. 1944.

A case of granuloma inguinale with metastatic osteolytic involvement of the left clavicle, right scapula, right sixth rib, and left tenth rib as demonstrated by roentgenographic examination is reported. Subcutaneous abscesses, 2 of which were followed by deep ulcers, had occurred over each of the sites of bone involvement. The initial lesion occurred on the cervix uteri and spread, involving the vulva. Ulceration of the left groin, considered to be the result of lymphatic spread from the vulval lesion, was also present, but the metastatic lesions appeared before involvement of the vulva and groin. The patient was a Negro woman, 21 years of age, who first began to have pain following a trivial injury in the upper sternal region in October 1942. Small tender masses appeared over the medial end of each clavicle, followed by the other lesions. Her constitutional symptoms became more severe and she was admitted, acutely ill, to the New Orleans Charity Hospital in February 1943. Blood serologic reactions for syphilis were negative.

Donovan bodies were abundantly demonstrable in all ulcerative lesions. Biopsies of rib, subcutaneous tissue and skin showed characteristic pathologic findings of granuloma inguinale.

On March 8, 1943, therapy was begun with diramin, a trivalent antimony compound (one cc. of the solution contains 8.5 mg. of antimony). The initial dose was 1 cc., followed by gradual increase to 5 cc. Systemic and local improvement began almost immediately but progressed slowly. The patient was ambulatory for a month before her discharge from the hospital on May 24, 1943, and treatment with diramin was continued in the outpatient department. No toxic effects of the drug were observed.



**The diagnostic implications of aortic insufficiency.** Louis Hammon. Cincinnati J. Med., 25: 95-120, May 1944.

Syphilitic aortic insufficiency is discussed as one of the eight groups into which the author divides cases in which a diagnosis of aortic insufficiency was made. About 80 percent of the cases occur between the ages of 30 and 60 years. There is a definite relation between the age at which syphilis is acquired and the age at which the symptoms of the aortic insufficiency appear. The duration of life following discovery of the disease averages from 3 to 4 years. If after treatment the patient leaves the hospital free of symptoms, it can be expected that he will be back with a return of symptoms after 2 or 3 months.

Syphilis affects only the aortic valves producing aortic insufficiency. Occasionally a patch of syphilitic disease will extend from the aortic valves to the anterior cusp of the mitral valves, but the author says he has never seen such an extension deform the valve so as to produce mitral insufficiency or stenosis. In well developed aortic insufficiency, a mitral systolic murmur nearly always is heard and usually also a presystolic murmur, the Austin Flint murmur. In many instances it is impossible to distinguish these murmurs from those produced by structural diseases of the mitral valves. Therefore, in the presence of aortic insufficiency caution must be used in gaging the significance of mitral murmurs. The aortic lesions of syphilis do not produce a high degree of aortic stenosis. A systolic murmur is always heard in the aortic area but the circulatory manifestations are those of aortic insufficiency. When evidence discloses a preponderance of stenosis over insufficiency, the aortic lesion is not syphilitic.

The serologic tests for syphilis are not absolute and unerring indications of the disease; repeatedly negative reactions occur in from 10 to 15 percent of cases of syphilitic aortitis. There are occasions when other evidence is so convincing that the aortic insufficiency may be considered as not syphilitic even when the serologic tests are positive.

It is a characteristic feature of syphilitic aortitis that the aorta becomes dilated; therefore, in doubtful cases dilatation of the aorta is a point in favor of syphilis. The association of syphilitic disease of the valves and bacterial endocarditis is not rare; it occurs more often than formerly was supposed. Dissecting aneurysms that travel downward to the root of the aorta often distort the ring and produce a high degree of aortic insufficiency.

The author discusses several interesting cases in which syphilis was a factor of the incorrect diagnosis.

**Syphilitic paroxysmal haemoglobinuria.**

James F. Hughes. M. J. Australia, Sydney, 2: 503, Dec. 18, 1943.

A case of a 22-year-old member of the Royal Australian Air Force who was seen at the service hospital in Sydney is reported. His personal history was negative for acquired syphilis and he had none of the clinical features of congenital syphilis. His father had amyotrophic lateral sclerosis, but his mother and only sibling were well.

He had been well until, on being transferred to Canada in the winter, he passed bloody urine after becoming very cold. When a similar incidence occurred 4 days later he was returned to Australia. Questioning disclosed that when the patient was between the ages of 5 and 12 years he had 6 or 7 such occasions each wintertime when he became extremely cold and he also had abdominal cramps. Between the ages of 12 and 21 years he remained well.

The Wassermann reaction was positive and the Donath-Landsteiner test for the detection of the specific autohemolysis in the blood was positive. The urine was examined after an attack and found to be dark red and to contain hemoglobin and methemoglobin.

**Generalized exfoliative dermatitis due to sulfadiazine.** Roswell D. Johnson. J. A. M. A., Chicago, 124: 979-980, Apr. 1, 1944.

The author is reporting a case of severe dermatitis due to sulfadiazine, probably the most extensive reported with recovery.

The patient was a boy 10 years of age who was treated for pneumonia with a not unusual dosage of 2 gm. (0.85 gr. per pound) sulfadiazine daily for 9 days. The drug was stopped after this because of a rash on his face and arms and a temperature of 102.5° F.

He was admitted to the hospital, acutely and seriously ill, on the twelfth day. A morbilliform rash covered the entire body, with numerous large blebs over the neck, shoulders and arms. There was a very severe conjunctivitis with purulent discharge, chemosis and photophobia. An ulcerative bleeding gingivostomatitis was present. It was impossible for the boy to take any significant quantity of fluid by mouth. Because of the close resemblance between the skin of the patient and that seen in a severe scald, he was treated as for a burn, petrolatum strips being applied, overlaid with gauze packs and fluffs, and an elastic bandage wound over all. Supportive treatment was given of intravenous drip containing dextrose, to which were added ascorbic acid, thiamine and niacin, and 1,100 cc. of pooled plasma and 625 cc. of fresh whole citrated blood. New blebs appeared daily for 8 days, and a progressive granulocytopenia was present. Ten units of crude liver extract was given intramuscularly in divided doses with equivocal success. By the ninth hospital day he was better and was discharged from the hospital on the twentieth day with new skin over the blistered areas and the mucous membrane greatly improved.

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## TREATMENT

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**How penicillin and sulfanilamide are pronounced.** Hosp. Management, Chicago, 57: 92, Apr. 1944.

Dr. Charles E. Funk, editor of the Funk & Wagnalls dictionaries, is quoted as saying that the word penicillin should be pronounced "pen-i-cil-lin" with major accent on the third syllable and lighter stress on the first syllable. He writes that he entered this pronunciation in 1942 after consulting with the New York

Academy of Medicine, the American Chemical Society, and Professor Fleming, the English scientist who discovered penicillin and gave it its name. The pronunciation "pen-iss'il-in" has not been accepted.

He also stated that most scientists agree that the proper pronunciation of sulfanilamide is "sulf-án-ul-a-mide" with the accent on the second syllable and the last syllable pronounced "mide" not "mid." The nontechnical pronunciation "suf-anil'-a-mide" seems to be growing, and it may be accepted on the basis of usage.

### Penicillin in the treatment of syphilis.

News and Comment. Bull. U. S. Army M. Dept., Carlisle Barracks, No. 75: 22, Apr. 1944.

In collaboration with the Penicillin Panel, Subcommittee on Venereal Diseases of the National Research Council, the Army, Navy, and U. S. Public Health Service are conducting studies to evaluate the effects of penicillin in the treatment of syphilis. The evidence accumulated to date indicates that penicillin has definite value in the treatment of this disease. In the Army, two treatment centers have been established, one at Fort Bragg, N. C., and the other at Camp Howze, Tex., where, under the supervision of specially qualified personnel, individuals with early syphilis are treated with penicillin. Particular attention is being focused on immediate response to the drug, to the proper time-dosage relationship, and to the percentage of clinical and serologic cures following the various dosage schedules. Because of the importance of close and accurate observation of each case treated, special procedures have been established to assure a minimum follow-up period of 12 months.

At present, the optimum dosage schedule has not been determined. Primary and secondary lesions respond quickly to the drug and ordinarily the serologic test is rapidly reversed, but sufficient time has not elapsed to assure the permanence of these results. For this reason the treatment of syphilis with penicillin will be limited to the two designated centers until more information is available.



**Penicillin treatment of resistant gonorrhea.** *Medicine and the War.* J. A. M. A., Chicago, 124: 991, Apr. 1, 1944.

"Because of the adequacy of supplies of penicillin available to the Army, persons with sulfonamide resistant gonorrhea will not be transferred to general hospitals for treatment except when indicated by complications, according to the Technical Bulletin of Medicine, No. 16, issued by the War Department recently. Station hospitals should requisition any additional supplies of penicillin needed for this purpose from the nearest general hospital. Penicillin will be administered to persons with gonorrhea immediately after failure to respond to one course of a sulfonamide compound. There is still insufficient evidence to justify the use of penicillin in any of the venereal diseases other than gonorrhea, and it will not be used for such treatment except when specifically authorized by the Surgeon General."

**Penicillin treatment of sulfonamide resistant gonococcic infections in female patients: Preliminary report.** Alfred Cohn, William E. Studdiford and Isaak Grunstein. *J. A. M. A.*, Chicago, 124: 1124-1125, Apr. 15, 1944.

Forty-two adult female patients with proved gonococcic infection who had not responded to at least two courses of sulfathiazole were treated at Bellevue Hospital with various amounts of penicillin. The other female patients were also given penicillin because they were sensitive to sulfonamides. The dosage varied from totals of 50,000 Oxford units given in 2 doses to 100,000 units in 5 doses. Of the 44 women, 43 became bacteriologically negative after treatment and remained negative during the follow-up period. Only 1 patient showed a relapse, following 2 doses of 25,000 units; she responded to an additional 100,000 units given in 4 doses.

The bacteriologic reversal took place as a rule within 12 hours following the termination of therapy.

A total dosage of 75,000 Oxford units appears to be satisfactory for the treatment of sulfonamide resistant gonorrhea in the adult female. The therapy may

be completed within 6 hours. No toxic effects from the penicillin were observed.

Eleven of the 44 patients suffered from a concurrent infection with *Trichomonas vaginalis*, which remained entirely unaffected by this type of therapy.

A child 5 years of age with a sulfonamide resistant gonococcic vaginitis was given 4 single doses of 10,000 Oxford units at 3-hour intervals. She promptly became negative and remained so during a follow-up period of 25 days.

**Penicillin therapy of gonorrhea in men.**

Charles Ferguson and Maurice Buchholtz. *J. A. M. A.*, Chicago, 125: 22-23, May 6, 1944.

A study was made on 753 patients treated with penicillin. The patients were all young, healthy men of the Merchant Marine and enlisted personnel of the Coast Guard, their chief disability being gonorrheal urethritis. All had failed previously to obtain a cure following some form of sulfonamide therapy in amounts varying from 20 to 500 gm.

At first the intravenous route was tried on 5 patients, but the result was not considered satisfactory and the intramuscular route was adopted. The details of the dosage are shown in a table, in which the patients were divided into 11 groups according to dosage rates. Of the 753 treated, 29 were considered as failures, a percentage of 4. From the 3 groups which showed no failures it is indicated that a total of 100,000 units or more is necessary to produce a cure, and also that 5 to 6 injections are necessary. In a group of 387 patients the total dosage was 80,000 units due to limitation of the drug; the results were excellent, showing only 3 percent failures.

The dosage necessary to produce a cure is 20,000 units per dose for 6 injections, making a total of 120,000 units. This was shown in 42 cases with no failures. The next best group was 381 patients treated as follows: 20,000 units for the first dose, then 10,000 units for the next 4 doses, and finally 20,000 units for the sixth and last dose, a total of 80,000 units. The result was a little over 2 percent failures.

The patients treated unsuccessfully were eventually cured as follows: Four

were treated with a combination of chemotherapy plus fever therapy. Five patients responded after a second course of penicillin. One patient required a third course, a total of 175,000 units divided into 25,000 units.

There was no immediate or delayed reaction noticeable from the drug.

**The treatment of resistant gonorrhea with induced hyperthermia supplemented by sulfonamide therapy.** John H. Harrison, Thomas W. Botsford and Frederick P. Ross. *J. Urol.*, Baltimore, 51: 215-227, Feb. 1944.

The authors have previously reported on a cabinet for the induction of hyperthermia which they designed and constructed at the 105th General Hospital. (A description of this cabinet is published on page 210 of this journal.)

The authors report their results with the first 300 patients with resistant gonorrhea treated with this cabinet in combination with sulfonamide therapy. All the patients had resisted chemotherapy. Equally good results were obtained by using either sulfathiazole or sulfadiazine, giving 5 gm. during the 18-hour period preceding treatment. A detailed description of the use of the cabinet is given.

Of the 300 cases of resistant gonorrhea treated by combined fever (a temperature of 106° F. for 7 hours) and sulfonamide therapy, 253 were cured, 22 were improved but not cured and 25 failed. Of the 253, 203 were cured by one treatment; 42 by a second course; 5 by a third course and 3 required four courses of treatment. One of the patients reported cured died 2 weeks after fever therapy, which was the only death to occur in 426 treatments administered to 300 patients. The 22 improved cases were later discharged as cured following further local and sulfonamide therapy. The duration of the disease was from 1 to 24 months. The average time of hospitalization following cure of gonorrhea by fever therapy was 13 days. The tests of cure were made during this hospitalization period, usually 3 to 4 days following fever therapy. Upon discharge the patient was returned to full military duty.

With the exception of the one death caused by combined hepatic and renal failure, the only other complications encountered were 10 cases of transitory hepatitis which subsided completely within 2 weeks after treatment.

**Correlation of in vitro sulfonamide resistance of the gonococcus with results of sulfonamide therapy.** Charles M. Carpenter, Helen Ackerman, Millard E. Winchester and Jane Whittle. *Am. J. Pub. Health*, New York, 34: 250-254, Mar. 1944.

A study was carried out at the Glynn County Board of Health, Brunswick, Ga., on the results of treatment with sulfathiazole on 105 patients with gonococcal infection and the in vitro response to sulfanilamide and sulfathiazole of the strains of the gonococcus isolated from these patients.

*Neisseria gonorrhoeae* was isolated prior to sulfonamide therapy of the 105 patients with gonococcal infection. Of this group, 88 (84 percent) were considered cured with one course of 20 gm. of either sulfathiazole or sulfapyrazine; 17 (16 percent) failed to be cured with the same amount of drug.

Seventy-seven (87.5 percent) strains of the gonococcus isolated from the 88 cured patients failed to grow in vitro in any of the concentrations, 5, 10, 20 and 40 mg. percent sulfanilamide, or in concentrations of 1, 2, 5 and 10 mg. percent sulfathiazole. The remaining 11 (12.5 percent) resisted the action of one or both drugs in vitro. Thirteen (76.5 percent) strains of the gonococcus from the 17 patients who failed to be cured remained viable when exposed to the same concentrations of sulfanilamide and sulfathiazole in vitro; 4 (23.5 percent) strains did not survive the drugs.

A correlation between the curative effect of the drugs in vivo and the resistance of the specific organism in vitro showed that 95 percent of the patients with nonresistant strains were cured in 5 days with 20 gm. sulfathiazole, and 46 percent of those with resistant strains responded to an equivalent amount of sulfonamide therapy.



During a 15-month period from May 42 to August 1943, of a total of 214 rains of gonococcus isolated prior to eatment and tested for sulfonamide resistance, 74 (34.6 percent) were resistant sulfanilamide and sulfathiazole in tro. Of especial interest is the finding at only 15.2 percent of these strains sted during the first 6 months of the udy were resistant, whereas observations made during the last 3 months owed that 59.3 percent of all strains ere resistant.

**new technique of prophylaxis in venereal disease.** Thomas G. Tousey, Emanuel J. Richter, Carl Glazer and Harvey Abramson. Bull. U. S. Army M. Dept., Carlisle Barracks, No. 75: 108-110, Apr. 1944.

An experiment with a new technic of prophylaxis in venereal disease was carred out on two regiments of about 1,000 en each. A modification of the technic sed by Loveless and Denton was used, nsisting of 2 gm. of sulfathiazole by outh given at the time of issuing a ass, 2 gm. when the pass was returned e following morning, and 2 gm. on the orning of the third day.

The test regiment had an incidence of cases of chancroid, while the control egiment reported 9 cases of gonorrhea nd 3 of chancroid during the same period f time. During the second part of the udy the regiments were reversed, and e control regiment was used as the test egiment. The results of this study howed an incidence of 1 case of chanroid in the test regiment, while 5 cases f gonorrhea and 2 of chancroid were reorted in the control regiment.

The authors believe these experiments rove the value of sulfathiazole prophylaxis against gonorrhea. It seems of less alue against chancroid. This method is f benefit only in case of troops going on ass for 24 hours or less.

**Neurological emergencies.** Charles D. Aring. South. M. J., Birmingham, 37: 230-235, Apr. 1944.

In acute syphilitic meningitis the cerebrospinal fluid usually shows an increased pressure, a pleocytosis of varying degree,

an increased protein content, a normal or moderately decreased sugar and chloride content, an abnormal colloidal gold reaction, and a positive Wassermann reaction. The condition usually develops within the first 2 years after the appearance of the chancre.

Syphilitic meningitis responds well to arsenotherapy. Treatment should be begun at once with 0.04 gm. mapharsen or 0.3 gm. neoarsphenamine intravenously. Three days later a second dose of 0.06 gm. mapharsen or 0.6 gm. neoarsphenamine is given, to be repeated every 6 days until a total of 20 injections are given. Coincident with the last intravenous injections of the arsenical, 2 cc. of bismuth may be given intramuscularly and repeated weekly until 10 or 20 doses have been given. Then mapharsen should be given weekly and alternated with bismuth until the cerebrospinal fluid is completely normal. The cerebrospinal fluid is examined every 4 to 8 months.

Tryparsamide may be substituted for mapharsen at the end of 1 year of treatment if there has not been a marked reduction in the cerebrospinal fluid abnormality.

If, following a year of tryparsamide and bismuth therapy, little progress is seen fever therapy may be resorted to in cases of syphilitic meningitis.

**Some complications of therapeutic hyperpyrexia.** Harry S. Etter. Arch. Phys. Therapy, Chicago, 25: 154-163, Mar. 1944.

The author points out some of the complications of artificially induced fever in the treatment of sulfonamide resistant gonorrhea or syphilis of the central nervous system. Hemorrhage, circulatory collapse and heat stroke are among the more serious complications. Among the minor complications are mentioned apprehension and restlessness, herpes simplex, and nausea and vomiting.

The potential and actual dangers of hemorrhage are described. The author suggests the routine administration of dextrose both by mouth and parenterally before treatment, especially before the longer 8- to 10-hour sessions, in an effort to build up the glycogen supply of the

liver and thus protect this organ as much as possible. Oxygen should be administered continually throughout all fever sessions. It is given by means of the nasal catheter at a rate of flow of 6 to 8 liters per minute. By this means a great deal of the restlessness and excitement can be prevented, possibly renal damage with the resultant dangers of hemorrhage can be obviated, and the hazards and sequelae of anoxemia may be avoided.

Circulatory collapse is usually the result of dehydration. The symptoms are the same as those observed in circulatory collapse from any other cause. If an intravenous drip of 5 percent solution of dextrose in physiologic salt solution is started with the first suggestion of this complication the treatment can be continued in many cases.

The cause of heat stroke is not definitely known, but apparently there is a derangement of the heat regulating center, possibly due to anoxemia or small hemorrhages about the center. The patient should immediately be removed from the cabinet and cooled by means of a tepid sponge bath and by a fan which blows cool air directly on his body.

Despite the low mortality rate, it should always be remembered that therapeutic hyperpyrexia is a potentially dangerous procedure, and the theory of when in doubt take the patient out of the cabinet should be followed.

**Impaired sexual ability following fever or therapeutic procedures.** Russell A. Winters. *Clin. Med.*, Waukegan, 51: 40, Feb. 1944.

The author points out that too often treatment is prescribed which may cause temporary or permanent injury to the male sexual organs. Trauma and high temperatures due to infection can raise the temperature of the testes and produce a secondary glandular change due to deficiencies of both the internal and external secretions. In these cases, ice bags or cold compresses should be used. The same condition exists when therapeutic artificial fevers are used.

The abuse of physical therapy methods such as short wave, diathermy, and hot sitz baths by too frequent, too long, or

too careless treatments can reduce the testicular activity, either temporarily or permanently. The testes should be protected from the electric current in these cases.

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## PATHOLOGY

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**The relationship of congenital syphilis to abortion and miscarriage, and the mechanism of intrauterine protection.** A. Louis Dippel. *Am. J. Obst. & Gynec.*, St. Louis, 47: 369-379, Mar. 1944.

The author made a study on 68 fetuses of nonsyphilitic and 67 of syphilitic women. These fetuses were autopsied and certain tissues examined for the presence of spirochetes. Only fetuses which had not reached viability were included in the study.

Fetal syphilis was diagnosed upon the discovery of spirochetes in fetal organs. The perivascular tissues of the liver and lungs generally yielded the largest number of spirochetes. The long bone, placenta, and umbilical cord were least satisfactory for the search of spirochetes.

A typical *Spirochaeta pallida* were found in 3 macerated fetuses from missed abortions. That the observed organisms were dead or dying spirochetes was proved by comparison with the changing forms seen in an aging darkfield preparation.

Spirochetes found in the tissues of fetuses from syphilitic mothers were morphologically like the *Spirochaeta pallida* and were considered as such since no spirochetes of any form were seen in the fetuses of nonsyphilitic mothers. Sixteen (23.9 percent) of the 67 fetuses of syphilitic mothers showed spirochetes in the tissues, which demonstrates the role played by syphilis in the production of abortion and miscarriage in this series. Fourteen (33.3 percent) were in 42 fetuses of Wassermann-positive mothers and 2 (22.2 percent) in 9 fetuses of Wassermann-negative mothers, showing that negative serologic findings following anti-syphilitic therapy is no assurance against congenital syphilis.



Spirochetes were not found in fetal tissues prior to the eighteenth week of gestation, which is considered the abortion period. The incidence of fetal infection with spirochetes rose from 10 percent in the first one-half of the miscarriage period to 50 percent in the latter half of the period, with the highest incidence (66.7 percent) in the twenty-sixth week.

The author concludes from these findings that there is some natural protection of the fetus against syphilis during the first 17 weeks of pregnancy. Wassermann-positive mothers must receive therapy before the eighteenth week if their fetuses are to be guarded against syphilitic infection, and both Wassermann-positive and negative women must have therapy before the twenty-third week, or approximately 50 percent of their offspring can be expected to be infected before viability is reached.

Evidence is offered to show that the Langhans' layer of chorionic epithelium affords appreciable protection of the fetus against the invasion of the *Spirochaeta pallida*, even after the sixteenth week of gestation. At this late stage it is in the form of delayed delamination and differentiation of the Langhans' cells.

**An etiological study of 1,036 cases of organic heart disease.** Aaron H. Traum. M. Bull. Vet. Admin., Washington, 20: 377-388, Apr. 1944.

An analysis was made of the main etiologic factors concerned in 1,036 (840 white and 196 Negro men) cases of organic heart disease in 2 midwestern Veterans' Administration Facilities over a period of 5 years. The average age of these patients was 48.93 years, ranging from 35 to 91 years.

Of the entire group, 55 (5.31 percent) cases were classified as due to syphilis, 26 (3.09 percent) in white and 29 (14.80 percent) in Negro patients. The criteria for diagnosis of syphilitic heart disease required the presence of the characteristic valvular findings of aortic insufficiency, and one or more of the following historical evidences of clinical findings: a history of a syphilitic chancre; a history of a positive serologic finding in the past;

a history of antisyphilitic treatments; a positive blood serologic reaction, and evidence of syphilis involving another part of the body.

Of the group of Negro patients, 13 admitted knowledge of a syphilitic chancre, 2 with positive serologic reactions admitted having positive blood tests and antisyphilitic treatments in the past, and 14 denied any knowledge of a syphilitic infection.

Approximately the same historical and laboratory findings were noted in the group of white patients with syphilitic heart disease. Thirteen admitted knowledge of a syphilitic chancre, 2 denied a chancre but admitted a positive blood test with antisyphilitic treatments in the past, and 10 denied syphilitic infection. Three of the men in this group gave a rather definite history of rheumatic fever in childhood as well as a history of a syphilitic infection as young men.

The Negro group revealed a comparatively high incidence of syphilitic heart disease, while the white group was surprisingly low. Thirty-four (63 percent) of the 55 patients were in the fifth decade of life. The average age of the white men was 46.73 years, ranging from 38 to 62 years, while the average age of the Negro men was 47.65, ranging from 41 to 68 years.

By comparing the author's findings with two similar studies of other sections of the United States, a lower incidence of syphilitic heart disease is seen in the white group in the midwestern study than in the groups from the Pacific Coast and from around the District of Columbia.

**A massive aneurysm of the innominate artery. A case with fatal termination from slow external rupture.** Rustom J. Vakil. Indian M. Gaz., Calcutta, 78: 587-588, Dec. 1943.

A 50-year-old Muslim man was admitted to the K. E. M. Hospital, Bombay, on Aug. 14, 1942, complaining of a painful swelling in the right side of the neck. There was a history of primary chancre 30 years before, followed by a generalized skin rash, with sore throat, adenitis, malaise and pains in the joints. Two months previous to admission to the hospital he

noticed pain in the neck and upper part of the chest on the right side and a small swelling, which progressively increased in size, in the right lower part of the neck above the clavicle.

Examination revealed a tumor about 3 to 4 inches in diameter with expansile pulsation, a systolic thrill and a systolic murmur. The patient was more comfortable in the semi-sitting position. The blood Kahn reaction was positive. Fluoroscopy revealed a normal aortic arch with a large aneurysmal swelling on the right side corresponding to the position of the innominate artery. The trachea was slightly displaced to the left.

Except for a progressive increase in the size of the lump, his condition remained stationary for a month after admission to the hospital. After that he showed progressively increasing dyspnea, respiratory distress, and intense and agonizing pain in the region of the aneurysm and along the right arm which persisted in spite of treatment by rest in bed, restricted diet and antisyphilitic drugs.

Examination on Dec. 3 showed the patient in much distress. The swelling was over 10 inches in diameter, extending over the neck and the upper part of the chest. There were ulcerations on the skin over the swelling, and on Dec. 15 the ulcerated patches began slowly to exude blood, which continued for 3 days. The patient died after having lost several pints of blood.

The author believes that this is probably the largest aneurysm of the innominate artery on record.

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## LABORATORY RESEARCH

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**Effect of yeast and yeast products on complement of guinea-pig serum.** S. D. S. Greval, S. N. Chandra and B. C. Das. *Indian M. Gaz., Calcutta*, 79: 16-17, Jan. 1944.

Due to climactic conditions, guinea-pig serum is of no value for use in complement fixation tests during the greater

part of the year in Calcutta. The heat causes it to lose its titer and become cholesterol shy. The authors have found that the use of marmite, yeast tablets and vegemite will correct these defects.

A group of 100 animals were given 4 teaspoonfuls of marmite daily for the first few weeks, then 2 teaspoonfuls daily. Both the defects disappeared within 2 weeks, and by adding marmite to the food did not appear again for 5 years.

Experiments were also made on another group of 100 animals using yeast tablets and vegemite. Nearly normal complement was obtained in some of these animals. The authors give a table showing their results in experiments covering a period from June to September 1941 and 1943.

**The in vitro effect of penicillin on sulfonamide resistant and sulfonamide susceptible strains of gonococci.** Alfred Cohn and Irma H. Seijo. *J. A. M. A., Chicago*, 124: 1125-1126, Apr. 15, 1944.

The authors conducted experiments to determine whether the combined antibacterial action of sulfathiazole and penicillin would be effective when the action of each individual agent was not sufficient to kill off the organism. The technic followed was identical with that previously described for the in vitro differentiation of sulfonamide susceptible and resistant strains, with the difference that penicillin was substituted for sulfathiazole. A total of 259 tests were performed on 55 sulfonamide resistant strains and 132 tests on 27 sulfonamide susceptible strains.

In a 1:10,000 dilution of penicillin representing 0.176 Oxford unit per cubic centimeter, all of the sulfonamide susceptible and resistant strains were killed off. With increasing dilutions of penicillin, sulfonamide susceptible strains were relatively more inhibited than sulfonamide resistant strains. The susceptibility of different strains to penicillin varied strikingly in different dilutions. The growth of sulfonamide resistant strains was not affected by the combination of "subtherapeutic" doses of penicillin and sulfathiazole.



The addition of para-aminobenzoic acid to various penicillin dilutions did not yield consistent results as to the growth effect on the gonococcus strains.

The antibacterial action of dilutions of penicillin obtained from stock solutions which were kept for 4 weeks at ice box temperatures and tested at weekly intervals did not reveal any essential variation of its potency.

**Action of penicillin and other antibiotics on *Treponema pallidum*.** Wolcott B. Dunham, Dorothy M. Hamre, Clara M. McKee and Geoffrey Rake. *Proc. Soc. Exper. Biol. & Med.*, Utica, 55: 158-160, Mar. 1944.

Preliminary tests employing penicillin in vitro, with 240 Oxford units per 0.8 ml., failed to reveal any action on the spirochetes. In tests in which the drug was used in still higher concentrations there was a relatively sharp increase in the action on the spirochetes between a concentration of 800 and 1,600 Oxford units per 0.8 ml.

The results obtained with certain other antibiotic substances showed that gliotoxin had a marked spirocheticidal action; aspergillic acid and bromo-aspergillic acid were less effective, and fumigacin was the least active.

The results of certain studies with penicillin on the prophylaxis of syphilitic skin infections in rabbits clearly showed that the strain obtained from the insufficiently treated rabbit was more resistant to the action of penicillin than was the original Nichols strain. The tests in which 1,600 Oxford units were present in 0.8 ml. of final mixture showed that 62 to 81 percent of the spirochetes of the unaltered Nichols strain were immobilized, while only 6 to 18 percent of the penicillin-fast spirochetes were rendered immotile. This finding indicates that in the treatment of human syphilis, care must be exercised to administer a sufficient quantity of penicillin to cure the patient rapidly; otherwise, there will be the possibility of producing a penicillin resistant strain.

**Studies on penicillin. I. Production and antibiotic activity.** Clara M. McKee, Geoffrey Rake and A. E. O. Menzel. *J. Immunol.*, Baltimore, 48: 259-270, Apr. 1944.

In an attempt to evaluate a method of assay of the potency of penicillin the authors developed two methods in their laboratory which they compared in accuracy and ease of performance with those already reported by other authorities. *Staphylococcus aureus* was the most common organism used.

The authors describe the serial dilution test which they found to be the simplest and most satisfactory for rough determinations on solutions of entirely unknown potency. *S. aureus* was the standard culture used. Into each of a series of 13 x 100 mm. tubes is put 0.5 ml. of a beef extract broth without added glucose. Of the solution to be tested 0.5 ml. is added to the first tube, and after thorough mixing 0.5 ml. is carried on to the second tube, repeating this procedure until all tubes contain twofold dilutions. The tenth tube will contain a dilution 1,024 times greater than the starting dilution. The culture (0.5 ml. of a  $10^{-6}$  dilution of a 6-hour growth containing approximately 500 organisms) is then added to each tube. After shaking, the tubes are incubated for 16 hours at 37° C. The activity of the unknown is determined by comparison with the standard, the end point being the last tube which, at 16 hours, shows complete inhibition of growth. Penicillin preparations can be sterilized by Seitz infiltration, since this produced no reduction of potency.

Another test which can be used when the approximate potency of a solution is known and a more accurate determination is desired is described by the authors.

It has been found that the stability of a calcium salt and a sodium salt of penicillin may be preserved for comparatively long periods of time at different temperatures when dried from the frozen state and sealed in vacuo in ampules which are stored in the ice box at 0° C.

The more purified preparations of penicillin have been found to have a con-

siderable activity against gram-negative bacilli.

#### **Filter paper disc modification of the Oxford cup penicillin determination.**

James G. Vincent and Helen Whitgrove Vincent. *Proc. Soc. Exper. Biol. & Med.*, Utica, 55: 162-164, Mar. 1944.

The authors describe their filter paper disc modification for the Oxford cup method for determining the potency of penicillin. They feel the modification should reduce the labor and time involved in setting up this test, while the ease with which extra replicates may be run should increase the test's accuracy. The principal modification is in the use of a thick filter paper disc saturated with the penicillin sample, substituted for the sample-containing small cylinder used in the Oxford cup method.

The disc method has been found to work equally well on blood serum, spinal fluid, and urine. As in the original Oxford method, no filtration of the sample is necessary under ordinary circumstances.

#### **A method for standardizing penicillin.**

Dorothy H. Heilman. *Am. J. M. Sc.*, Philadelphia, 207: 477-483, Apr. 1944.

A method is described for the standardization of penicillin in which a determination is made of the amount of penicillin necessary to prevent the growth of pneumococci in semisolid tissue culture medium. The principal advantage of this method is that it is not necessary to use a standard preparation in the performance of the test. The amount of penicillin needed for a determination of potency is small. The accuracy of the method appears to compare favorably with that of the Oxford method in a limited number of tests. Repeated tests with the same sample of penicillin indicate that the variation of the results obtained is fairly small.

Preparations of penicillin from different sources have been standardized by this method. Results obtained, as well as tests done elsewhere, indicate that the actual potency of a product may be significantly different from the estimated potency at the time of preparation.

**A method for the estimation of sulfanilamide and its derivatives in biologic fluids.** C. S. Jang and W. S. Cheng. *Chinese M. J.*, Washington, 61: 227-232, July-Sept. 1943.

Because many of the reagents used in the current methods for the estimation of the sulfonamides were not available, the authors have devised a method which requires only reagents which are generally obtainable in China. Various modifications of this method, with the use of still simpler reagents and devices, have been worked out so as to be adaptable to small hospitals and clinics under the present wartime conditions.

The method for the estimation of the drug in the blood is described as follows: Run exactly 2 cc. of blood slowly from the pipet drop by drop into 16 cc. of 5 percent trichloroacetic acid with constant shaking of the container. Filter through a dry filter paper. Transfer exactly 9 cc. of this filtrate into a test tube. Add 1 cc. of 0.5 percent sodium nitrite. Mix well. Then add 2 cc. of 0.5 percent thymol in 20 percent sodium hydroxide. The orange color developed is compared with that of the standard solution of sulfanilamide, sulfapyridine and sulfathiazole (1 or 2 mg. percent), freshly prepared from a stock solution of 0.1 or 0.05 percent in concentration by means of a suitable colorimeter (the authors use the Duboscq type). Where trichloroacetic acid is not available alcohol may be used, with a slightly different procedure.

For determination in urine, the urine is generally diluted to 1 : 20 by introducing 5 cc. of urine into a flask, adding 1 cc. sodium hydroxide and then finally diluting to 100 cc. This is filtered, and exactly 5 cc. of the filtrate is transferred into a test tube, and 2 cc. of 1N hydrochloric acid and then 1 cc. of 0.5 percent sodium nitrite are added. This is mixed well and 2 cc. of 0.5 percent thymol in 20 percent sodium hydroxide are added. The color is compared with that of the standard.

In places where the colorimeter is not available, some simple device such as a block comparator may be used though at the expense of sensitivity.



actors in the resistance of gonorrhea to sulfonamides. Walter T. Goodale and Louis Schwab. J. Clin. Investigation, New York, 23: 217-223, Mar. 1944.

Experiments were carried out whereby here was developed a rapid method of identifying sulfonamide resistant strains of gonococci with sufficient accuracy to permit prediction of the possible success of sulfonamide therapy in any given case. Pure cultures of gonococcus were isolated and incubated. At 18 hours standard suspensions of the growths were made in buffered saline, pH 7.4, and serial tenfold dilutions were then made in similar saline. A drop of 6 suspensions (standard and 5 dilutions) was placed in turn, each upon a marked sector of a starch agar petri plate. The drops of inoculum were then merely placed upon the medium. The plates were incubated and examined at 18 hours. From a study of the growths and of the control plate, it was possible to express the results of sulfonamide inhibition in vitro as 2 factors—a resistance index and as maximum dilution.

In 32 cases of male gonorrhea which were studied, it was possible to predict the clinical course that would follow treatment with sulfonamides. It was found that a "typing" of the organisms into responsive and resistant groups could be obtained with accuracy by the use of one plate containing 1 mg. percent of each sulfonamide.

The conclusion drawn theoretically was that whether or not the initial and prompt cure with sulfonamides will be obtained at all seems to depend upon a contest between organism and drug in a relatively neutral host. Correlation between clinical and in vitro resistance of the infecting strain to sulfathiazole and sulfadiazine was demonstrated in every case studied. This correlation indicates that those factors within the gonococcus which determine in vitro resistance to sulfonamides also determine whether the infection will respond promptly and permanently to sulfonamides, or show varying degrees of clinical resistance. Host

factors appear to be relatively unimportant, except in those infections in which the course is initially unaffected by drug therapy.

The in vitro resistance of the organism, and hence the clinical response to be expected under sulfonamide therapy can be accurately estimated by this method. It is suggested that such in vitro methods have a possible application in other bacterial infections.

**On the growth requirements of *Neisseria gonorrhoeae*.** R. Gordon Gould, Lewis W. Kane and J. Howard Mueller. J. Bact., Baltimore, 47: 287-292, Mar. 1944.

It has been generally believed, although without valid evidence, that the gonococcus requires complex substances, such as ascitic fluid, blood or serum, for growth. The authors report on their investigation of growth factors.

The starch casein-hydrolyzate meat-infusion medium of Mueller and Hinton was used as a basis and the attempt was made to eliminate or replace each constituent with known compounds. It was found that freshly isolated strains would grow without meat infusion although the colonies remained very small. None of a large number of vitamins, bacterial growth factors or other substances tested were able to replace the meat-infusion factor, either singly or in various combinations.

By replacing the casein hydrolyzate in the basal medium with mixtures of pure amino acids, it was found possible to obtain growth in a medium consisting of glutamic acid, histidine, glucose, starch, glutathione, magnesium and iron salts, phosphates, sodium chloride, and agar. Casein hydrolyzate and meat infusion contain unknown factors which greatly stimulated the growth on this medium but which were not essential. Evidence was obtained showing that the function of starch in the growth of the gonococcus is a protection against the inhibitory effect of certain samples of agar.

**Lesions in rats given sulfathiazole, sulfadiazine, sulfanilamide, sulfamerazine, sulfapyrazine, or acetylsulfadiazine in purified diets.** K. M. Endicott, A. Kornberg and F. S. Daft. *Pub. Health Rep.*, Washington, 59: 49-54, Jan. 14, 1944.

Six hundred and sixty rats were examined, of which 300 had been given sulfadiazine, 170 sulfathiazole, 70 sulfanilamide, 60 acetylsulfadiazine, 19 sulfapyrazine and 18 sulfamerazine. Twenty-three control rats were given one of the purified diets without sulfonamides.

The bone marrow, skeletal muscle, cardiovascular system, liver, spleen, kidney, adrenal and thyroid were examined for lesions. The following lesions occurred with some or all of the drugs: Depletion of mature granulocytes in the bone marrow with or without an increase in nucleated red cells; necrosis and calcification of skeletal muscle; calcification and hyalinization of pulmonary, coronary, and renal arteries; hydropic degeneration and hyaline necrosis of the liver; necrosis and hemorrhage of the adrenal cortex; hyperplasia of the thyroid; hemorrhage into subcutaneous tissue, body cavities, and various organs; hemosiderosis of spleen, liver, and renal tubules; renal intratubular sulfonamide deposits with varying degrees of tubular damage.

Hemorrhages into subcutaneous tissue, body cavities, and various organs with no demonstrable vascular lesions occurred in rats given sulfadiazine, sulfathiazole, sulfamerazine, or sulfapyrazine. They showed a very prolonged prothrombin time. Vitamin K prevented the hemorrhages and reduced the prothrombin time to normal levels. A detailed report on these findings will be made later.

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## **PUBLIC HEALTH ADMINISTRATION**

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**Venereal disease: Conviction of infected person exposing another by sexual intercourse to venereal disease.** J. A. M. A., Chicago, 124: 1082, Apr. 8, 1944.

An Oklahoma statute makes it a felony for any person after becoming infected

with venereal disease and before being discharged and pronounced cured by physician, to marry or expose any other person to such disease by sexual intercourse. The petitioner was charged with having had sexual intercourse with stated person while she was infected with a venereal disease. She had pleaded guilty and had been sentenced to the State penitentiary. Later a habeas corpus proceeding was instituted in the criminal court of appeals of Oklahoma alleging that the information had been defective and insufficient in that it failed to negate the fact that she had been "discharged and pronounced cured by reputable physician in writing," which, it was alleged, the statute specifically makes an element of the offense.

In a former similar case (*Eppe v. State*), the court held it to be fundamental that it is not necessary in an information to allege any fact which it is not necessary for the State to prove to secure a conviction. Under the statute involved if the State had the burden of proving that the accused had not been discharged and pronounced cured by a reputable physician in writing, it would create an almost insurmountable burden on the State. To the court it was apparent that this provision was inserted in the statute by the legislature as a matter of defense which may be interposed by an accused and when such defense is made, it then should be submitted to a jury for the determination as to whether the accused had been discharged as cured by a reputable physician and had innocently exposed another person under the honest belief that she was no longer infected. The State would have the burden of proving beyond a reasonable doubt that the accused had become infected and that subsequently she had exposed another person to such disease.

The court accordingly held that the information filed in the trial court was sufficient to allege a violation of the statute and that the commitment of the petitioner of a plea of guilty was sufficient authority for her confinement in the penitentiary. The writ of habeas corpus was accordingly denied.



**venereal disease control in Texas.** Reports from the State Health Department. Texas State J. Med., Fort Worth, 39: 633-634, Apr. 1944.

From the examination of the first 2,000 Selective Service registrants it is found that Texas stood sixth from highest in syphilis rates in the United States.

The Division of Venereal Disease Control immediately intensified their control measures and at present the following principles are in effect: (1) The operation of free diagnostic and treatment clinics for indigent patients. (2) The distribution of free drugs to private physicians for treatment of indigent and semi-indigent patients. (3) The operation of rapid treatment centers for treatment of highly infectious cases. (4) The operation of a central registry for clearance and referring all reports on venereal disease cases and their contacts. (5) The operation of a case-finding and case-holding program. (6) The maintenance, analysis, and interpretation of statistics on venereal disease services rendered which is used as a basis for future program planning. (7) The operation of a venereal disease public health educational program. (8) A service of consultation and advice to private physicians on the treatment of nonindigent and semi-indigent patients.

At present, there are 148 clinics operating in Texas, treating 40,000 cases of syphilis. There are four rapid treatment centers operating in the State, and plans for establishing four more centers are under way. The division has launched an extensive venereal disease public health educational program designed to reach all levels of society with information concerning the prevention, the cause, the spread, and the cure of the venereal diseases.

**Wartime consideration of syphilis.** Paul A. O'Leary. Illinois M. J., Chicago, 85: 132-137, Mar. 1944.

The author discusses the work being done in the control of venereal diseases in different parts of the United States and in the Army and the Navy.

On the basis of reports available, the State of Illinois anticipates 30,150 new cases of syphilis during 1943, of which 5,000 will be new or acute infections. In 1942, 28,675 cases of syphilis were reported in Illinois. During 1943, Illinois will spend approximately \$1,260,000 to maintain 116 venereal disease clinics, and to provide drugs, consultation service, serologic tests, education and training of personnel and maintenance of case-finding and case-holding records.

At present there are five systems of treating acute syphilis being used in hospitals, army camps and venereal disease clinics in all parts of the United States. The evaluation of these methods is now being made, and the author believes that in 3 years the value of the procedures can be determined. From experience thus far it appears that 1,200 mg. of mapharsen, given by either the continuous drip method or by syringe, in 5 to 12 days, offers the highest incidence of cure and the lowest percentage of complications.

**The control of venereal disease in Oregon—I and II.** W. H. Aufranc. Oregon Health Bull., Portland, 22: 3-4 and 3, Mar. 29 and Apr. 5, 1944.

Oregon has made a great deal of progress in its venereal disease control program. Clinics staffed with trained personnel have been established in all areas in which there are large military concentrations. Local and State financial assistance has been secured in each of these areas, so that no person who needs treatment for a venereal disease may fail to secure it either from a private physician or from a public health clinic, and all case-contact investigations may be started promptly to prevent the transmission of the disease to others. In parts of the State where there is no large military problem, free drugs and epidemiologic service are furnished to private physicians. These programs are flexible enough to fit any type of postwar program for continuing the fight against venereal disease.

Recent legislation in Oregon has removed the "indigency clause" from the law concerning the testing of blood for

syphilis by the laboratories of the State Board of Health, so that physicians may now have blood tests made on any patient without charge.

Oregon feels that stringent law enforcement is not wise. Case-finding, case-holding, and contact-investigation procedures are considered as prerogatives of public health workers.

To date, 95 percent of all selectees in the State having a positive blood test have been satisfactorily handled.

Venereal disease educational programs are also being provided. The Portland City Health Bureau has sponsored a program of venereal disease education for shipyard workers and senior high school students. Educational efforts in the shipyards are through movies, lectures and literature. A spot survey for 1 month during 1943 indicated that about one-third of all the persons applying for diagnostic and treatment services at the Portland Public Health Clinic were influenced to do so as a result of the educational efforts in the shipyards. The program in the high schools appears to have met with general approval and a definite amount of success, so that it is now a part of the regular high school curriculum.

#### **Plan for reaching industrial workers through industrial health committees.**

Percy Shostac. *J. Social Hyg.*, New York, 30: 58-66, Feb. 1944.

With the object of evolving an instrument with which to achieve an employee-management cooperation on behalf of a comprehensive and permanent health education program, in which venereal diseases played a large part, an Industrial Health Committee was formed in the Fort Greene-Bedford District of Brooklyn, New York. This is a highly industrialized section of Brooklyn in which more than 200 important plants and firms are located, including many war production plants and the Brooklyn Navy Yard. It is anticipated that 150,000 workers will be reached through this program. Organized as well as unorganized labor groups are included. The first meeting, in which representatives of industry, unions, the Navy, the New York City Health Department and the American Social Hygiene

Association participated, was held about 6 months ago and to date almost 60 of the largest firms have affiliated.

On the basis that education is a cornerstone of preventive medicine, the Committee is convinced that well informed men and women will take the necessary steps to avoid health hazards and to seek early treatment when illness occurs. Through teamwork on the part of workers and management, the program will endeavor to make the Fort Greene-Bedford District industrial community health conscious. The program includes the publication and distribution of a semimonthly illustrated health tabloid, the intensive use of posters, placards, pamphlets, movies and lectures, and active health committees within each firm.

The author suggests a procedure which may be utilized by interested communities.

#### **Syphilis and gonorrhea in 1943. Quart. Bull., Dept. of Health, New York City, 11: 49-51, Dec. 1943.**

Comparative figures are given, covering the first 10 months of 1941 and the first 10 months of 1943, of primary or secondary syphilis and early latent syphilis reported in New York City. An increase is seen in every instance, the highest being in the 15- to 19-year age group of 132.1 percent for early infectious syphilis and 108.3 percent for the early latent syphilis. The 20- to 24-year age group showed an increase of 73.2 percent of primary or secondary syphilis. Gonorrhea cases among the early age groups showed similar increases.

In 1941, 33.3 percent of all reported cases of early syphilis were 15 to 24 years of age, whereas in 1943 the rate has increased to 46 percent.

The need for venereal disease education is indicated from these findings. Although the health department has the legal authority, the necessary services for those who cannot afford a private physician and educational materials for an intensive antivenereal disease program, its efforts will be of no avail without the help of private physicians, parents, the church and other community agencies.



# New Cases of Syphilis and Gonorrhea in States, Territories, and Possessions

Health officers' monthly statement: Reported for the first 9 months of fiscal years 1943-44 and 1942-43

Area	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital		1943-44	1942-43
	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43		
U. S. †	1341,770	1421,627	257,690	262,197	292,084	2110,090	3145,628	3182,895	210,004	212,323	2128,737	2199,748
Alabama	13,346	16,167	1,734	2,581	3,043	4,571	3,168	4,835	281	398	4,853	6,696
Arizona	2,061	1,861	476	269	570	413	811	1,019	99	90	1,303	749
Arkansas	7,641	13,009	934	1,371	2,565	5,057	2,976	5,251	162	220	3,445	3,651
California	25,102	23,403	4,128	3,269	5,806	5,152	13,967	13,390	733	684	25,924	17,740
Colorado	3,043	3,819	732	732	861	916	1,334	2,004	116	167	2,453	1,876
Connecticut	2,180	2,160	253	203	982	672	480	749	71	80	1,161	1,081
Delaware	751	833	120	100	201	202	185	217	17	22	169	124
Dist. Col.	6,298	(*)	721	(*)	1,466	(*)	3,825	(*)	107	(*)	2,866	(*)
Florida	21,532	26,826	2,414	3,224	6,890	6,718	9,705	13,509	456	605	12,360	10,248
Georgia	11,877	21,335	2,374	2,927	4,774	10,132	4,363	7,709	361	566	7,613	9,409
Idaho	406	341	182	101	72	23	117	169	8	17	624	249
Illinois	20,743	21,830	2,821	2,486	4,738	4,431	12,763	14,348	421	565	17,564	14,767
Indiana	6,504	10,420	987	1,301	612	254	2,435	4,054	188	343	2,622	3,494
Iowa	1,850	2,166	356	259	491	699	809	978	121	75	1,348	1,354
Kansas	2,205	2,959	454	595	456	341	1,213	1,429	82	84	1,442	2,057
Kentucky	5,383	10,098	845	1,218	1,172	2,165	2,274	4,344	207	312	2,705	3,427
Louisiana	13,551	13,100	2,310	1,830	3,524	3,796	3,554	6,092	357	364	10,705	5,185
Maine	818	696	168	164	113	108	418	305	80	67	1,037	504
Maryland	10,870	13,488	1,256	926	1,266	1,084	2,331	1,561	96	156	5,253	5,964
Mass.	4,400	4,117	891	712	(§)	(§)	3,239	3,214	268	189	3,867	3,422
Michigan	12,800	14,242	1,897	1,423	3,340	2,212	5,451	4,511	317	360	8,499	6,606
Minnesota	1,861	2,297	179	175	206	236	1,352	1,755	90	80	1,457	1,132
Mississippi	19,566	30,317	6,650	7,419	5,560	10,259	6,535	11,492	817	1,147	22,194	24,796
Missouri	7,734	7,457	1,329	1,170	1,999	1,478	3,752	3,598	252	188	4,472	3,430
Montana	322	374	81	120	50	26	128	180	7	7	236	254
Nebraska	1,005	1,631	145	187	449	377	345	981	27	55	1,100	1,280
Nevada	583	596	34	(*)	96	(*)	398	(*)	18	(*)	281	204
N. Hampshire	213	245	31	23	49	20	110	171	13	19	137	145
New Jersey	8,460	8,458	993	1,013	2,563	2,195	4,545	4,876	336	275	3,975	5,095
New Mexico	1,541	1,712	324	301	373	330	767	951	67	84	1,075	558
New York	27,366	28,095	4,071	2,922	4,823	4,383	17,343	17,661	766	960	14,549	12,160
N. Carolina	8,525	13,499	2,228	2,809	3,462	5,624	2,679	4,738	156	328	6,823	8,452
N. Dakota	236	246	78	30	40	40	65	114	18	13	204	187
Ohio	17,416	17,997	2,746	2,570	4,203	4,165	8,986	10,470	700	792	4,289	3,432
Oklahoma	6,042	8,179	793	1,214	1,688	3,211	2,226	1,919	222	223	3,897	3,458
Oregon	1,543	1,099	472	208	113	103	907	708	51	63	1,914	985
Pennsylvania	10,080	4,922	1,346	902	3,761	2,897	3,691	(*)	486	94	614	(*)
Rhode Island	811	833	76	29	85	63	574	646	18	27	611	381
S. Carolina	11,796	15,186	2,472	3,200	4,703	6,334	4,089	5,063	268	327	4,973	4,332
S. Dakota	381	400	67	71	69	139	191	148	28	18	282	215
Tennessee	14,037	18,166	1,804	2,361	5,702	6,028	6,046	9,150	309	428	10,523	8,078
Texas	18,801	36,940	2,415	4,534	5,733	7,496	7,748	11,827	584	1,352	8,258	12,817
Utah	657	447	165	149	88	47	390	239	14	8	460	596
Vermont	205	199	60	104	67	0	68	86	9	9	153	142
Virginia	11,239	13,860	3,122	4,065	4,232	4,937	3,538	4,364	201	292	9,295	6,381
Washington	3,236	(*)	654	(*)	695	(*)	1,440	(*)	99	(*)	6,067	(*)
W. Virginia	2,709	4,271	496	649	462	738	659	1,206	93	141	1,715	1,783
Wisconsin	692	843	131	163	0	1	553	663	8	17	782	592
Wyoming	886	488	84	118	128	17	439	201	23	12	135	260
<i>Territories and possessions</i>												
Alaska	73	125	47	35	13	32	10	32	1	5	334	399
Hawaii	752	852	145	226	85	99	508	431	51	45	1,339	1,064
Puerto Rico	11,044	7,086	1,188	1,538	2,082	1,073	3,717	2,461	1,461	1,250	2,839	2,242
Virgin Is.	150	163	27	42	90	92	26	22	6	7	229	104
Actual total† of United States, Territories and possessions.	363,323	429,853	60,506	64,038	96,611	111,386	159,243	185,841	11,747	13,630	233,025	203,557

\*Data not available.

\*\*Includes "not stated."

†Based on States reporting in both fiscal periods.

‡Includes all reported cases.

§Included in late and late latent.

¹ Based on 47 States.

² Based on 46 States.

³ Based on 45 States.

# New Cases of Syphilis and Gonorrhea in Cities of 200,000 Population and Over

Health officers' monthly statement: Reported for the first 9 months of the fiscal years 1943-44 and 1942-43

City	Cases of syphilis and gonorrhea reported for first 9 months of fiscal years below											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital			
	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43
Total†	125,346	125,639	14,866	13,723	26,233	22,392	52,503	57,828	2,544	2,322	59,978	52,095
Akron	660	979	93	135	158	193	357	607	38	44	243	192
Atlanta	2,093	3,053	556	742	637	1,051	990	1,233	21	27	984	749
Baltimore	8,538	10,397	969	681	884	714	1,881	1,142	58	54	2,044	2,756
Birmingham	3,570	4,997	236	445	970	1,466	898	1,283	65	130	416	705
Boston	1,400	1,550	267	227	0	147	888	1,009	37	54	1,017	894
Buffalo	1,485	1,425	180	122	168	23	1,100	1,226	37	54	660	744
Chicago	11,867	12,505	1,931	1,730	2,808	2,542	6,891	7,907	237	326	9,993	9,671
Cincinnati	2,311	2,739	314	303	(§)	(*)	1,997	(*)	(*)	(*)	729	770
Cleveland	3,109	2,981	577	500	1,001	696	1,460	1,686	71	99	1,153	1,083
Columbus	1,213	1,198	254	151	272	244	633	762	34	41	258	305
Dallas	1,947	2,492	366	327	398	406	1,164	1,729	18	28	544	867
Dayton	1,325	943	144	140	367	167	771	598	43	34	540	206
Denver	1,489	1,760	329	333	401	326	557	1,012	45	47	1,354	868
Detroit	8,968	6,268	1,149	856	2,773	1,585	4,884	3,690	162	137	4,362	3,713
Honolulu	415	513	48	186	52	65	277	232	38	30	851	838
Houston	1,498	3,361	254	233	528	1,168	672	1,868	44	92	1,674	884
Indianapolis	1,696	3,163	428	470	79	67	412	747	20	29	92	398
Jersey City	361	531	37	41	79	84	237	385	18	21	33	42
Kansas City	1,367	1,568	237	223	255	206	822	986	49	65	757	722
Los Angeles	8,625	5,994	0	362	3,418	1,731	4,955	3,728	252	173	3,893	3,293
Louisville	1,562	2,000	269	241	283	353	666	1,204	21	47	688	983
Memphis	5,282	5,811	452	525	2,462	2,017	2,267	3,077	78	74	3,988	2,005
Milwaukee	373	432	39	64	5	5	313	357	3	6	142	91
Minneapolis	544	656	86	68	96	106	344	474	16	14	593	514
Newark	1,679	1,903	223	265	441	508	964	1,093	51	37	663	777
New Orleans	1,951	2,417	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	1,463	892
New York	19,049	19,965	3,447	2,704	4,266	3,702	10,621	12,377	469	531	10,524	8,523
Oakland	1,258	983	137	112	322	247	748	581	36	23	1,089	679
Oklahoma City	1,528	1,578	153	232	394	514	480	513	35	19	781	625
Omaha	437	864	41	94	221	164	146	561	20	34	368	548
Philadelphia	7,469	2,672	254	224	814	(*)	860	(*)	52	(*)	682	(*)
Pittsburgh	7,571	6,288	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	107	208
Portland	673	560	193	108	38	37	429	385	13	31	829	475
Providence	383	393	54	20	37	27	251	316	7	10	124	111
Rochester	211	244	42	28	14	1	150	206	5	9	221	179
St. Louis	4,682	3,108	601	393	1,540	951	2,382	1,676	149	88	1,533	755
St. Paul	222	387	26	41	36	49	142	273	10	13	225	146
San Antonio	932	1,323	129	103	243	336	523	816	28	52	1,008	720
San Diego	862	795	84	84	253	265	457	433	30	12	748	522
San Francisco	2,258	2,630	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	1,643	2,325
Seattle	1,038	1,022	143	131	185	136	647	681	16	16	1,304	1,046
Syracuse	738	665	20	18	23	2	674	629	21	16	246	139
Toledo	707	526	104	61	126	91	450	346	27	27	94	132
Washington, D. C.	6,298	(*)	721	(*)	1,466	(*)	3,825	(*)	107	(*)	2,866	(*)
Actual total‡	131,644	125,639	15,587	13,723	28,513	22,392	59,185	57,828	2,481	2,544	63,526	52,095

\*Data not available.

\*\*Includes "Not Stated."

†Based on cities reporting in both fiscal periods.

‡Includes all reported cases.

§Included in late and late latent.

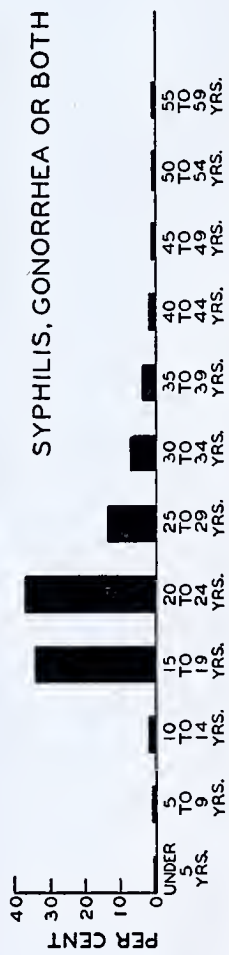
1 Based on 43 cities.

2 Based on 40 cities.

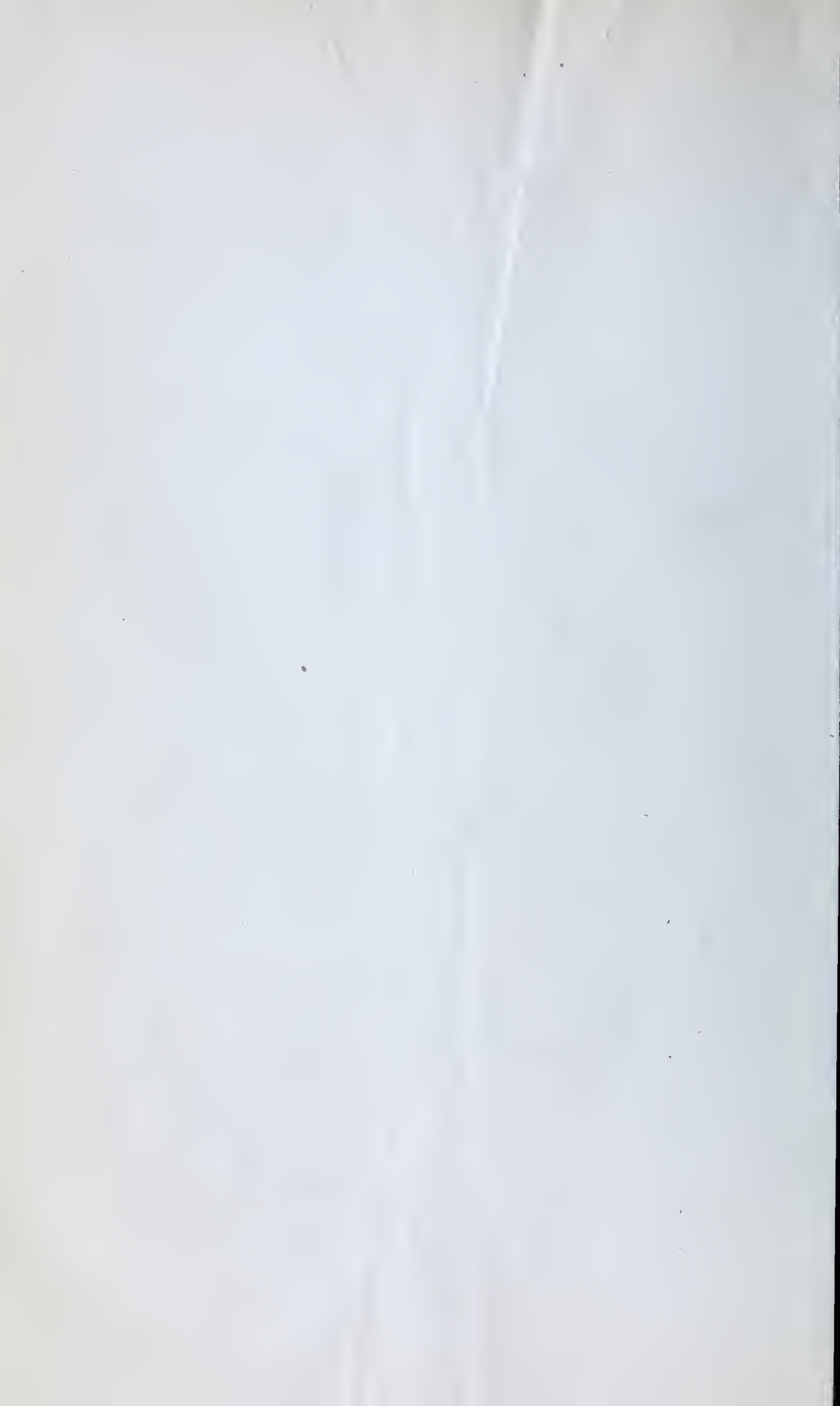
3 Based on 38 cities.

4 Based on 42 cities.





CUMULATIVE PER CENT DISTRIBUTION OF ADMISSIONS TO RAPID TREATMENT CENTERS FOR VENEREAL DISEASES ACCORDING TO AGE AS OF APRIL 30, 1944





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**FEDERAL SECURITY AGENCY  
UNITED STATES PUBLIC HEALTH SERVICE**

**THOMAS PARRAN, *Surgeon General***

**Editor: J. R. HELLER, Jr., *Medical Director*  
*Chief, Venereal Disease Division***

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# Outpatient Penicillin Treatment of Gonococcic Infections in Males

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United States Public Health Service

The purpose of this report is to present the results obtained by the use of outpatient penicillin therapy of male patients with gonorrhea. It appears to have been demonstrated (1,2,3,4) that sufficient amounts of penicillin given over a time interval of 2 or more hours produced a high cure rate. Since the demands on the private physician and on the clinic personnel cannot readily provide these long periods of treatment on a continuing basis, it was considered advisable to evaluate the efficacy of penicillin on gonorrhea when the product was administered within the span of an 8-hour working day.

The patients comprising the two series under report were active seafaring males, generally healthy except for the gonococcic infection, and ranged from 17 to 43 years of age—the average being 22 years. About 80 percent of the patients were white. Approximately two-thirds of these men had been treated previously with ample amounts of sulfonamide compounds without success. In some instances the disease had been present for several months before the start of penicillin treatment. The members of the group under active therapy were required to be at the clinic only at the times designated for the intramuscular injections. Interdiction of sexual intercourse during the period of study was the only restriction placed on these patients.

All patients accepted for inclusion in this study were required to have both clinical evidence and cultural proof of the gonococcic infection. Beyond these demands selection of patients was not practiced.

All penicillin was administered intramuscularly in the upper and outer quadrant of alternate gluteal areas. The penicillin employed was a solution of the sodium salt

in distilled water. Concentration of the penicillin sodium solutions ranged from 8,000 to 10,000 Oxford units per cubic centimeter. These solutions were kept at 3°-5° C. and were not warmed before injection. Injections were made with a #22 gage, 1½ inch needle. The patients were requested to return to the clinic daily, except Sunday, until discharged from post-treatment observation. They were instructed not to void for at least 2 hours before each post-treatment examination. On each visit observations as to the absence or degree and character of the urethral discharge and a note on the two-glass urine test were recorded. The urethral discharge was streaked directly on the surface of the culture medium (5). When it was no longer possible to strip out any urethral discharge the centrifuged urine sediment was used as the inoculum. Later in the post-treatment period the prostate gland was very gently massaged previous to the collection of the urine specimen for culture study. Every effort was made to continue the follow-up examinations for at least 8 days. Except in the instances of obvious failure a specimen for the culture detection of gonococci was taken at each visit.

The series under report is comprised of two groups. Group 1 consisted of 114 patients and group 2 of 65 patients. The members of group 1 received intramuscular injections of 2 cc. of penicillin sodium solution containing 8,000 Oxford units per cubic centimeter—16,000 units per dose—at 9:00 a.m., 11:30 a.m., 2:00 p.m., 4:30 p.m., and again at 9:00 a.m. the following day. Thus within a span of 7½ hours 64,000 Oxford units were administered followed by an interval of 16½ hours before the final dose of 16,000 units was given to make a total dosage of 80,000 Oxford units.

The patients in group 2 received 25,000 units intramuscularly at 9:00 a.m., 11:30

From the Venereal Disease Research Laboratory, Staten Island, N. Y., and from the U. S. Marine Hospital, New York, N. Y.

a.m., and 2:00 p.m., and 50,000 units as a final treatment at 4:30 p.m. The total amount of penicillin sodium administered to members of group 2 was 125,000 Oxford units given within a period of 7½ hours.

The criteria of cure are considered minimal from an investigative viewpoint. The requirements were that (a) the post-treatment period continue for a minimum of 8 days, (b) there be complete subsidence of all clinical evidence of the disease by the time of release, (c) a minimum of 3 cultures be taken and all post-treatment cultures be negative. In group 1 the average post-treatment observation period was slightly more than 10 days; the maximum, 18 days. The average number of negative cultures was 7; the maximum, 9. In group 2 the maximum period of follow-up was 14 days and the average was 9 days. The maximum number of cultures for test of cure was 8, the average being 5.

The results obtained in the two groups will be presented separately. Of the 114 patients treated in group 1 the results are evaluated in only 93 instances since 21 of the patients did not return for a sufficient period or did not have enough culture examinations. Twelve of the 93 patients failed to respond while 81 completely satisfied the demands of the criteria, yielding a cure rate of 87 percent. The 21 patients who lapsed post-treatment observation were all clinically and culturally negative when last seen. Five of these patients had been observed for 7 days, 3 for 6 days, 3 for 5 days, 2 for 4 days, and 4 for 3 days.

Of the 12 failure cases in group 1 one patient was so classified because of a persistent urethral discharge although repeated culture examinations did not reveal gonococci. One patient developed an acute unilateral epididymitis, and a positive urethral culture was found on the third post-treatment day. Four patients had positive cultures on the second day, 3 on the sixth day, 2 on the seventh day, and 1 on the tenth day. Nine of these 12 failure cases returned to the clinic for further treatment. Larger dosages of penicillin administered over a longer period were uniformly successful in eradicating the infection.

Twenty-two of the 65 patients in group

2 lapsed the post-treatment observation requirements, thus leaving the results in 43 patients to be considered. Of these 43 patients, 36 (about 84 percent) responded satisfactorily to the treatment while the remaining 7 patients were cultural and/or clinical failures. Of the 7 failure cases 1 was so considered solely on clinical evidence, 2 had positive cultures on the second day, 2 on the fourth day, 1 on the fifth day, and 1 on the sixth day. The 22 lapsed cases were apparently cured when last examined. Four of these patients had been followed for 7 days, 4 for 6 days, 6 for 5 days, 3 for 4 days and 3 for 3 days.

Neither failure to respond to sulfonamide therapy, duration of the disease, nor race appeared to have any determining effect on the response to penicillin therapy in either group.

Many of the patients in each of the two groups volunteered the information that a definite sense of well-being followed the injections of penicillin. There was not any evidence of toxicity, and the few instances of irritation upon injection of the penicillin solution were related directly to the product employed, the penicillin having a very pronounced odor of amyl acetate or related compounds.

One patient with a concomitant syphilitic chancre developed a slight Herxheimer reaction on the day of treatment.

Although dysuria and frequency of urination cleared quickly in patients who were cured, it seemed that possibly the urethral discharge tended to disappear more slowly than in patients responding satisfactorily to sulfonamide therapy.

The results presented indicate that the intramuscular injection of penicillin sodium solutions, as employed in the series under report, produced a fairly satisfactory number of cures and that the use of either method or modifications thereof may permit the more widespread application of penicillin treatment to the problem of gonorrhea control. By analogy to the results of other agents employed in the treatment of gonococcal infections it may be reasonable to assume that the penicillin treatment regimes for men, as reported here, may be of value in the treatment of this in-



fection in women. This is not considered as proved.

It is well to recognize that the criteria of cure which accept a minimal post-treatment observation of only 8 days leave much to be desired. This period of follow-up was adopted only as a practical solution to the very vexing problem of case holding and patient control. The men in these two series were extremely anxious to return to their work at sea. Further there is every reason to suspect that numbers of these men did not cooperate, as requested, in abstaining from sex contact during the period of surveillance. On the basis of admissions by certain of the patients who returned even to the original source of the infection, valid doubt is cast on the records presented which listed as penicillin failures those clinically cured patients who, after a series of negative cultures, were found to have a positive culture on the sixth or seventh (and in 1 case, the tenth) day. This is a finding which was not encountered in penicillin treated gonococcal infections of patients hospitalized for 2 to 3 weeks for treatment and post-treatment observation, (2,3) and who were scrutinized by the same laboratory procedures in the same laboratory. The finding that the occurrence of positive cultures in "clinically cured" patients was followed in 2 to 4 days by a moderate to profuse gonococci-laden urethral discharge is of importance to those who do not have culture facilities.

It is noted that 43 of the total of 179 patients were listed as lapsing the post-treatment observation required by the criteria of cure and were not, for that reason, included in the determination of the cure rate. Since all of these men were apparently cured at the time of the last examination it may conservatively be concluded that the proportion of failures would not have been any greater, but perhaps less, for this group than for those who were followed for at least the minimum prescribed period.

In addition to the gonococcal urethral discharge each of 2 patients had a penile ulcer. The results of standard syphilis serologic tests were negative before treatment but darkfield examinations were not made until the day following the comple-

tion of the penicillin therapy. Darkfield examinations, made on 3 consecutive days, did not reveal the presence of the *Treponema pallidum* in the penile ulcers. After 10 to 14 days the blood tests for syphilis gave doubtful results which slowly increased to positive during the following 2 to 3 weeks. It has been shown that following the administration of penicillin the darkfield examination of syphilitic chancres becomes negative within 12 to 16 hours (6) and that early administration of penicillin (as in acute gonorrhea) may prevent the development of the primary lesion in concomitantly acquired syphilis, which is later manifested by a secondary eruption or by positive blood serologic reactions (7). It is therefore of the greatest importance to emphasize the necessity, (1) for darkfield examination of all suspicious lesions before starting penicillin therapy, (2) of emphatically warning the patient of a possible concurrent syphilitic infection, and (3) of the need for a physical and serologic examination at a later date or at the time of any untoward signs and/or symptoms.

#### *Summary and conclusions:—*

1. Penicillin sodium solutions administered intramuscularly to outpatients during a limited period on one or two days cured approximately 86 percent of male patients with gonococcal infections.

2. Evidence of toxicity was lacking.

3. Failure to respond to previous sulfonamide therapy, race, or duration of the infection did not appear to affect the response to penicillin treatment.

4. Penicillin treatment of gonococcal infections may interfere with the darkfield diagnosis or mask the development of a concurrently acquired syphilitic infection. Full cognizance must be accorded this fact.

5. The application of either regime of penicillin therapy presented, or substantial modifications thereof, may serve to make the use of penicillin for gonococcal infections more readily adaptable to use in outpatient clinics and in private practice.

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## A Consideration of Certain Factors of Importance in the In Vitro Determination of the Resistance of *Neisseria Gonorrhoeae* to the Sulfonamides and to Penicillin: Part I. Sulfonamide Resistance

J. H. Hill, M. E. Petroskas and S. V. Huffer

It is the opinion of many clinicians that resistance of gonococci to the sulfonamides has increased significantly. The gradual development of penicillin-resistant gonococci is to be expected if one may reason by analogy with the behavior of other organisms. In general it is probable that the increased incidence of resistance to any chemotherapeutic agent is chiefly due to two causes, the natural selection of normally resistant organisms and an actual increase of resistance in some cases receiving inadequate prophylactic or therapeutic treatment. In regard to the sulfonamides, too little work was done originally on natural differences of the resistance of gonococci, but both Boak and Carpenter (1) in the United States and Schmith and Reymann (2) in Europe showed that marked variations of resistance did exist in gonococci genealogically free from any exposure to these drugs. We can now measure only the present degree of sulfonamide resistance. In the case of penicillin and other antibiotics, there is still time to determine the base line of natural resist-

ance, so that accurate measurements of any increase of resistance can be made later if necessary. In any event, it is unfortunate that there has been no general agreement in regard to methods to be used in the study of drug resistance. Some standardization of laboratory technics for the determination of the resistance of gonococci to the sulfonamides and to the antibiotics is essential if the patterns of the development of resistance are to be followed both in different parts of the world and as the period of use of these agents lengthens.

Accurate in vitro determination of resistance necessitates the use of a medium which is free from substances which are inhibitory to the chemotherapeutic agent. The problem of obtaining such a medium appears to be much more difficult in regard to the sulfonamides than, as will be shown later, in the case of penicillin.

With the exception of the tests in human blood made by Cohn, Steer and Seijo (3) and by Cohn and Seijo (4) and the studies of Landy and Gerstung (5) determination of the in vitro resistance of gonococci to the sulfonamides has been made in media which utilize meat or peptone, both of which contain sulfonamide inhibitors. Fur-

From the James Buchanan Brady Urological Institute, The Johns Hopkins Hospital, Baltimore, Md.



thermore, no measurement of the amount of such inhibitors present in the media was made, although these varied widely with different investigators, (6, 7, 8, 9, 10, 11, 12, 13, 14).

While valuable parallels between *in vitro* and clinical resistance have been obtained by such means, these technics actually have not measured the exact degree of sulfonamide resistance but only that of such amounts of sulfonamide as might be present in a given medium in excess of that inactivated by the inhibitor. Although by use of a constant method effect of such excess of sulfonamide over inhibitor should remain the same, the findings of investigators employing different media, containing different and undetermined amounts of sulfonamide inhibitor cannot be compared. In view of the quantitative relationship between sulfonamide inhibitor and the drug there is no reason to doubt that while an excess of drug over inhibitor may be present, as at relatively high sulfonamide levels, if the amount of drug is not in excess of the quantity inactivated by the inhibitor, no determination of sulfonamide resistance can be made.

The determination of sulfonamide resistance is becoming a routine bacteriologic procedure. The object of this study has been to find a medium which can be prepared with relative simplicity for routine use and in which the amount of sulfonamide inhibitor has been reduced to a minimum. The complexity of the valuable medium prepared by Landy and Gerstung (5) makes its routine use difficult. We present here a modification of the cystine, dextrose, blood agar medium previously reported by Huffer and Hill (15). This was chosen for investigation because it lacks one inhibitor-containing ingredient, meat. The ingredients of this medium have been tested for the presence of sulfathiazole inhibitor by methods similar to those previously employed by Hill and Mann (16) and satisfactory modifications have been tested for the growth of the gonococcus.

#### METHOD

Sulfonamide inhibition was tested in the "SIGI" medium employed by Bliss and

Long (17). This was preferred to the medium used by MacLeod (18) because heavier growth was obtained in 24 hours. The medium was tubed in 5 ml. amounts, with addition of the test substance or its incorporation in the medium, and with appropriate controls. The inoculum consisted of 0.1 ml. of a  $10^{-4}$  dilution of an 18-hour culture of *E. coli*, grown in the same medium. The organism did not tend to dissociate in this medium. After 24 hours of incubation, serial dilutions were made in saline and duplicate plates were poured. Tests were run in triplicate, so that at least 6 plate counts were available for the determination of the counts for every variation. Turbidimetric methods could not be used in tests with blood. Moreover, we were primarily concerned with the number of viable organisms and had previously found that many population changes occurred at drug levels which permitted no visible growth. Since it is well recognized, as recently emphasized by Rantz and Kirby (19), that two factors are of importance in the determination of sulfonamide inhibition, (1) stimulation of growth by the substance being studied, and (2) actual interference with drug action, population counts were made in preparations without sulfathiazole and after the addition of graded concentrations of the drug.

The ingredients of the medium which have been analyzed are as follows:

1. Blood, human or rabbit, 8 ml. per 100 ml. of medium and unheated or "chocolated" after addition to the medium
2. Bacto-peptone, 14 gm. per liter
3. Primary potassium phosphate, 6.5 gm. per liter
4. Sodium chloride, 5 gm. per liter
5. l-cystine, 240 mg. per liter
6. Glucose, 5 ml. of 20 percent per 100 ml. of medium

No sulfonamide inhibitor was found by the addition of the potassium phosphate, sodium chloride, l-cystine or glucose in the amounts used. The two ingredients which required the most investigation were therefore blood and peptone. These will be considered separately.

# 1. Blood.—

MacLeod (18), by similar methods, could not demonstrate sulfapyridine inhibitor in 23 specimens of human serum from 16 pathologic subjects. He used 1.66 mg. per cent of drug. Our problem involved the determination of sulfonamide inhibitor in defibrinated human or rabbit blood, unheated or "chocolated," in the proportion of 8 ml. of blood per 100 ml. of medium.

A. Unheated human blood: On the day of collection this blood stimulated growth to 9.7 times that obtained in the blood-free control. No evidence of interference was observed. On the contrary, there was an increase of bactericidal effect, probably due to the combined action of blood and drug. After 6, 14 and 28 days this blood had lost most or all of its stimulating effect and except for some apparent interference

TABLE 1.—Findings in basic medium, with and without the addition of blood

Substance added to basic medium "SIGI"	Exp. No.	Inoculum	24-hour findings									
			Mg. percent of sulfathiazole									
			0		0.5		1.0		5.0		10.0	
			Esch./Ml.	Log	Esch./Ml.	Log	Esch./Ml.	Log	Esch./Ml.	Log	Esch./Ml.	Log
8 ml. saline/100 ml.	3	7,700	144,000,000	8.2	39,455	4.6	31,125	4.5	7,200	3.8	—	—
do	4	1,515	368,500,000	8.6	40,250	4.6	16,690	4.2	24,240	4.4	—	—
do	5	39,100	170,500,000	8.2	88,375	4.9	59,875	4.8	41,600	4.6	—	—
do	8	9,370	226,500,000	8.4	—	—	—	—	—	—	10,065	4.0
do	9	6,870	337,000,000	8.5	—	—	—	—	21,110	4.3	—	—
do	10	3,100	240,000,000	8.4	—	—	—	—	34,700	4.5	—	—
do	11	14,500	272,665,000	8.4	—	—	—	—	17,100	4.2	—	—
do	12	9,350	166,100,000	8.2	—	—	—	—	12,516	4.1	—	—
do	13	6,415	645,000,000	8.8	—	—	—	—	8,185	3.9	—	—
do	14	15,070	256,700,000	8.4	—	—	—	—	5,730	3.8	—	—
do	15	20,900	265,650,000	8.4	—	—	—	—	14,185	4.2	12,185	4.1
8 ml. fresh, defibrinated human blood, pooled as above, medium "chocolated"	3	7,700	1,397,000,000	9.1	38,650	4.6	1,125	3.0	—100	2.0	—	—
do	3	7,700	785,500,000	8.9	54,675	4.7	25,125	4.4	—100	2.0	—	—
8 ml. human blood, as above, 6 days old	4	1,515	607,000,000	8.8	117,875	5.1	30,336	4.5	1,580	3.2	—	—
do	4	1,515	470,750,000	8.7	62,375	4.8	27,750	4.4	540	2.7	—	—
8 ml. human blood, as above, 14 days old	5	39,100	130,350,000	8.1	41,225	4.6	480	2.7	570	2.8	—	—
8 ml. human blood, as above, 28 days old	8	9,350	395,413,500	8.6	—	—	14,500	4.2	—	—	—15	1.2
8 ml. fresh defibrinated rabbit blood, pooled as above, medium "chocolated"	3	7,700	1,331,650,000	9.1	2,807,190	6.4	631,230	5.8	36,215	4.6	—	—
do	3	7,700	(—10,000,000)	—	—	—	56,285	4.7	10,400	4.0	—	—
8 ml. rabbit blood, as above, 6 days old	4	1,515	510,650,000	8.7	2,642,500	6.4	1,330,000	6.1	13,400	4.1	—	—
do	4	1,515	614,000,000	8.8	2,666,075	6.4	455,250	5.6	2,000	3.3	—	—
8 ml. rabbit blood, as above, 14 days old	5	39,100	522,200,000	8.7	1,528,750	6.2	62,525	4.8	840	2.9	—	—
8 ml. rabbit blood, as above, 28 days old	8	9,350	750,000,000	8.9	—	—	688,750	5.8	—	—	11,165	4.0

Human blood was collected from 5 normal subjects and pooled in equal amounts; a similar pool was made with rabbit blood. The growth-stimulating and sulfathiazole interference of these pools were tested the day of collection and after 6, 14 and 28 days of refrigeration. Analysis of the findings, which are given in table 1, indicates the following results:

at 0.5 and 1.0 mg. percent levels of sulfathiazole in the 6-day tests, the statistical significance of which is questionable, no interference was observed.

B. "Chocolated" human blood: On the day of collection this blood stimulated growth less than the unheated blood but to more than 5 times that in the control. The only possible interference was observed at the



mg. percent level of drug. As with the unheated blood, at 6 days, little stimulation of growth was noted. Possible slight interference was observed at the 0.5 and 1.0 mg. percent levels of drug, but not at 5 percent.

C. Unheated rabbit blood: When fresh this exerted only slightly less stimulation, 0.2 times the growth in the control, than fresh human blood and it also showed some evidence of interfering action. Again, the stimulating effect had dropped markedly at 6, 14 and 28 days. At 6 days marked interference was observed at the 0.5 and 1.0 mg. percent drug levels, none at 5 mg. percent. Interference was also observed at the 0.5 mg. percent level at 14 days and

from Pfanstiehl's peptone by adsorption with 2 gm. of powdered charcoal<sup>1</sup> per 100 ml. of plain broth prepared with 10 gm. of this peptone per liter. Our problem was to remove the sulfonamide inhibitor from Bacto-peptone, employed in our medium in the amount of 14 gm. per liter. The findings, summarized in table 2, indicate that the removal of sulfonamide inhibitor from the Bacto-peptone was much more difficult than had been anticipated on the basis of MacLeod's findings with Pfanstiehl's peptone. Little effect was obtained by adsorption of Bacto-peptone with 28 gm. per liter of charcoal, the amount equivalent to the 20 gm. of charcoal per 10 gm. of peptone

TABLE 2.—The effect of charcoal adsorption upon the sulfonamide inhibition of Bacto-peptone

Amount of peptone per liter	Amount of charcoal adsorption		Exp. No.	Inoculum	24-hour findings					
	Gms./liter	No.			Mg. percent of sulfathiazole					
					0		5.0		10.0	
					Esch./Ml.	Log	Esch./Ml.	Log	Esch./Ml.	Log
14	0	-----	8	9,350	2,788,500,000	9.4	-----	-----	291,945	5.5
			10	3,100	1,343,000,000	9.1	-----	-----	-----	-----
			11	14,500	1,400,000,000	9.1	-----	-----	-----	-----
14	28 (*)	1	8	9,350	1,995,000,000	9.3	-----	-----	275,830	5.4
14	20 (*)	2	10	3,100	601,300,000	8.8	-----	-----	-----	-----
14	56 (*)	1	8	9,350	1,905,000,000	9.2	-----	-----	8,259,800	6.9
14	80	1	10	3,100	455,800,000	8.6	-----	-----	-----	-----
14	80	1	11	14,500	365,000,000	8.6	-----	-----	-----	-----
14	160	1	11	14,500	290,000,000	8.5	-----	-----	-----	-----
14	160	1	12	9,350	734,750,000	8.9	-----	-----	-----	-----
14	160	2	12	9,350	238,165,000	8.4	-----	-----	-----	-----
14	160	2	13	6,415	150,167,000	8.2	-----	-----	-----	-----
14	320	1	11	14,500	327,750,000	8.5	-----	-----	-----	-----
14	320	1	12	9,350	427,700,000	8.6	-----	-----	-----	-----
14	320	1	13	6,415	81,700,000	7.9	-----	-----	-----	-----
14	200	2	15	20,900	168,165,000	8.2	-----	-----	14,650	4.2

\* For controls in medium without peptone, see Table 1.

at the 1 mg. percent level at 28 days.

D. "Chocolated" rabbit blood: When fresh this exerted slight, if any, interference. At 6 days significant interference was noted at the 0.5 and 1.0 mg. percent drug levels, not at 5 mg. percent.

## 2. Peptone.—

MacLeod and Mirick (20) found that sulfonamide inhibitor could be removed

tested by MacLeod. By the use of gradually increasing amounts of carbon it was found that not until adsorption was made with 160 gm. of carbon used twice, 320 gm. used once, or finally 200 gm. used twice that results could be obtained at the 5 mg. percent level of sulfathiazole that were of

<sup>1</sup>Carbon, Decolorizing, Code 1551, General Chemical Co., New York, N. Y.

the order of growth in the controls.<sup>2</sup> The addition of 56 gm. of carbon per liter did not reduce the factor of growth stimulation observed in the medium made with unadsorbed peptone, but when 80 gm. or more of carbon were used, no significant growth stimulation was observed.

#### DISCUSSION

It is evident that generalizations in regard to the lack of sulfonamide inhibitor in blood should not be made, but that further investigation should be undertaken on the effect of different kinds and amounts of blood upon different levels of sulfonamides. In regard to the removal of sulfonamide inhibitors from peptones, it will be necessary to study the behavior of any given brand before any conclusions can be drawn concerning it. Evidently wide differences in the ease with which the inhibitor can be removed are to be expected. In testing the growth of gonococci upon the cystine, glucose, blood agar medium prepared with filtrates after peptone adsorption, changes in colony type have been observed with some strains, but the amount of growth has not been diminished.

#### SUMMARY

1. The necessity for some agreement on methods for the determination of the sulfonamide resistance of gonococci and for the use of media free from sulfonamide inhibitors has been discussed.

2. Human blood has been found more suitable than rabbit blood for use in a sulfonamide inhibitor free medium.

3. It has been possible to remove sulfonamide inhibitor from 14 gm. of Bacto-peptone per liter by adsorption with carbon in the following amounts, 160 gm. twice, 320 gm. once, or 200 gm. twice.

4. A modified cystine, glucose, blood agar medium has been prepared which is free from significant amounts of sulfonamide inhibitor and which may be used

routinely for the determination of the sulfonamide resistance of gonococci.

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<sup>2</sup>In these experiments the basic medium was prepared by use of the adsorption filtrates instead of water as diluents. Sulfonamides are adsorbed by the carbon and cannot be added until after adsorption.



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It is a pleasure to acknowledge the statistical advice of Dr. Margaret Merrell, School of Hygiene and Public Health, The Johns Hopkins University.

## Positive Culture Results for *Neisseria Gonorrhoeae* from Prostatic Secretions and the Culture Results from Urine Voided Before the Prostatic Massage

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Present day tests of cure for gonorrhea in the male consist of a series of cultures taken during the 3-month period following the cessation of clinical evidence of the disease. After prostatic massage, the urine, which then contains part of the prostatic secretion, is used as a specimen for gonococcal cultures. Sediments of urine voided before the prostatic massages are also used as specimens for such cultures.

The performance of prostatic massage requires definite skill. It should be done gently yet firmly enough to empty most of the lobules. Rough massaging may cause trauma. The stroking is done in order to free deep-seated gonococci. However, such stroking cannot be considered safe when gonococci are present because the secretion containing gonococci may be forced into the interstitial tissue and lymph spaces. After prostatic massage reinfections of the urethra by the patient's own gonococci have been observed. Prostatic massaging usually causes unpleasant sensations, and in mentally unstable patients it may even bring about psychic trauma.

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Voiding into a sterile tube is a simple and safe method. After considering the disadvantages of the first method of securing specimens for culture and the simplicity of the second method, it seemed worthwhile to compare the value of the two types of specimens in detecting gonococci by culture. An opportunity for such an evaluation was afforded since the laboratory of the Boston Dispensary performs simultaneous cultures of the prostatic secretion and of the sediment of urine voided before prostatic massage. The results of such simultaneous cultures and the time interval between negative and positive urine sediment cultures are presented.

The total number of prostatic secretion cultures carried out by the laboratory in 1943 was determined and classified according to positive and negative results. For each positive patient, the number of positive prostatic cultures was established, as well as the results of cultures from urinary sediments obtained before stroking the prostate. For the patients with negative urine cultures, the time intervals between the positive prostatic culture and the appearance of the next positive urine sediment culture were noted. The incidence of pus in spreads taken from the culture-positive prostatic secretions was determined.

*Incidence of culture-positive prostatic secretions.*—A total of 295 patients with gonorrhea were treated in 1943. In the same year the research laboratory cultured 1,682 samples of prostatic secretions for *Neisseria gonorrhoeae*. Of these, 1,626 (96.68 percent) were negative and 56 (3.32 percent) positive. Fifty-one of these positive specimens were accompanied by specimens of urine voided immediately before the prostatic massage.

The negative percentage is explained by the fact that a large majority of the patients not cured by sulfonamide therapy will show negative prostatic secretions if the first prostatic massage is postponed long enough for the stroking to be safe.

*Results of simultaneous urine sediment and prostatic secretion cultures.*—The 51 urine sediment cultures which had corresponding positive prostatic secretion cultures were positive in 45 instances and negative in 6.

*Time interval between the first negative urine sediment culture accompanying positive prostatic secretion culture and the next positive urine sediment culture.*—One of the 6 patients considered here did not return to the clinic; he had had, however, repeated positive urine cultures. Another patient, a carrier, did not show clinical nor bacteriologic signs of gonorrhea after the single positive prostatic culture. Therefore, dates can be given here only for the 4 remaining patients.

In 3 patients the interval between the first negative urine culture and the next positive was 7 days; in one patient this interval was 5 days.

Negative urine culture at a time when prostatic secretion culture reveals gonococci

generally does not persist. In all the active cases, a positive urine culture follows within a week. Carriers cannot be detected by urine cultures alone.

*Distribution of the positive prostatic secretions.*—There were 56 positive prostatic secretions among 31 patients. In two-thirds of these cases with positive prostatic secretions the presence of gonococci could be proved but once, while the remaining third demonstrated gonococci for a longer period.

*Results of microscopic examinations of spreads from culture-positive prostatic secretions.*—Neither in 1,628 spread examinations of culture-negative prostatic secretions nor in 56 spread examinations of culture-positive secretions were gonococci found.

Spreads of the 56 culture-positive prostatic secretions were reported as positive for pus in 25 specimens and negative in 31 specimens. As a rule, spreads from prostatic secretions with a single positive culture result did not reveal pus.

The spreads of 56 culture-positive prostatic secretions were negative. The finding of gonococci in prostatic spreads depends on the stage of the disease. Early stroking will result in a much higher percentage of positive spreads than will cautious stroking in the safe period.

The presence or absence of pus cells in the prostatic spread is no indication of the presence of gonococci in the prostatic secretion.

*Summary.*—In 295 patients treated for gonorrhea in 1943, culture tests of cure using urine sediments as culture specimens were, in general, as efficient as tests of cure using culture specimens from prostatic fluids.

## Prevalence of Gonorrhea Among Syphilitic Patients: A Study Made in Delaware in 1943

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Many syphilitic patients being treated in public venereal disease clinics have undiagnosed and untreated gonorrhea. It seems unreasonable to assume that gonorrhea will be detected to any great extent

in the general population if it is not discovered among the syphilitic clientele of venereal disease clinics conducted by trained clinicians.

A random survey made of 412 patients



attending venereal disease clinics sponsored by the Delaware Board of Health revealed some significant facts.

THE SURVEY

Of the 412 patients included in this survey 406 or 96 percent were Negroes. This is in keeping with the preponderance of Negro patients attending the venereal disease clinics. No patient was interviewed or examined more than once although occasionally a clinic was visited twice to interview previous "absentees."

After receiving antisyphilitic treatment all male patients were asked to report to the physician making the survey. Identifying data were first obtained. The patient was interrogated to determine whether he had ever had gonorrhea, and if so, at what age, how many times it had recurred, and from whom he had sought treatment. Because few of the patients understood the meaning of the word "gonorrhea" common synonyms were used, such as "the running ranes," "pussy discharge," "the clap," "a strain." Every patient who admitted having had one of these conditions was talked with until it was clear that he had a good understanding of the question. This was done to avoid confusing seminal emissions with gonorrhea.

Following this interview, an inspection of the penis was made by the examiner, who stripped the urethra with his gloved hand. If any discharge was visible, either purulent or mucopurulent in nature, a direct contact spread was made. If the discharge was scanty a second spread was made using a cotton-tipped, wooden applicator. No cultures were made because adequate facilities were not readily available.

The spreads were examined at the State board of health laboratory and they were reported as being positive or negative for gram-negative intracellular diplococci.

Since many of the patients interviewed reported the frequent recurrence of a urethral discharge, repeated examinations of the entire group would undoubtedly greatly increase the percentage found to be positive. Cultural methods would also have added to the list of diagnosed cases.

TABULATION

- 1. Number of patients attending clinics for syphilis interviewed and examined for urethral discharges ..... 412
- 2. Number who gave a positive history for gonorrhea..... 369
- 3. Number who gave a negative history for gonorrhea (5 in this group had urethral discharge which was positive for gonococci)..... 43
- 4. Ages at onset of gonorrhea (first attack) :

Age—Years	Number of cases	Percent of total
12-15	14	3.8
16-17	48	13.0
18-19	135	37.0
20-24	129	35.0
25-29	35	9.0
30-34	5	1.4
35-40	3	0.8

- 5. Number found to have urethral charge and spreads made..... 132
  - Number of spreads reported as positive for gram-negative intracellular diplococci ..... 82
  - Number of spreads reported as nonspecific ..... 50

- 6. Average number of recurrences:

Times	Cases	Percent
0	110	30
1	159	43
2	51	14
3	29	8
4	18	5

- 7. Percent of apparent cures:
  - Number of patients giving a positive history ..... 369
  - Number of patients having a discharge ..... 132

Number of patients asymptomatic 237  
or 65 percent.

SUMMARY

- 1. Of 412 syphilitic patients examined only once, 132 or 32 percent had a urethral discharge which warranted the making of a spread. Eighty-two (20 percent) of all the patients interviewed had a urethral discharge which was positive for gram-negative intracellular diplococci.
- 2. Of 412 syphilitic patients interviewed 369 or 89 percent admitted having a urethral discharge at an average age of 19

years. In 391 or 94 percent of these patients there was a history of recurrent discharge.

3. No patient was examined more than once for the purpose of this survey. No gonococcus cultures were made.

#### CONCLUSIONS

1. Gonorrhea was extremely prevalent in the group of syphilitic patients studied.

2. The presence of gonorrhea in many of these patients was undetected because of the clinicians' preoccupation with the treatment of syphilis or lack of interest in gonorrhea as a communicable disease.

3. Unsupervised ambulatory treatment of gonorrhea with the sulfonamides resulted quite often in an amelioration of symptoms but not in the permanent eradication of the disease.

4. This study suggests that the present methods of dealing with gonorrhea are ineffective from the standpoint of diagnosis, treatment and epidemiology.

Penicillin is proving to be an effective yet relatively nontoxic therapeutic agent in the treatment of gonorrhea. Treatment with penicillin can be telescoped into a period of hours rather than days.

It is therefore apparent that by providing a brief period of hospitalization for infectious gonorrhea patients during which penicillin can be rapidly administered in large doses, public health agencies can effectively break the present chain of infection in many places.

The expenditure of public funds to provide the required hospital treatment would represent a real public health "bargain."

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## DIAGNOSIS

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The problem of falsely doubtful and positive reactions in the serology of syphilis. John A. Kolmer. *Am. J. Pub. Health*, New York, 34: 510-526, May 1944.

An analysis is made of the results of nine serologic surveys begun in 1935, in-

cluding the 1941 Washington conference on serology.

While a large percentage of the falsely doubtful and positive reactions in the serodiagnosis of syphilis are found to be due to errors in the collection of blood, resulting in excessive contamination or hemolysis, and to faulty laboratory technic, there is some possibility of technical errors being inherent in the test itself, with the result that falsely doubtful and positive reactions may occur in the hands of skillful and experienced technicians. Of the 10 tests employed, the Kolmer alone has given negative reactions in all of the 9 serologic surveys with normal presumably nonsyphilitic serums. Through the efforts of the Committee on the Evaluation of the Serodiagnostic Tests for Syphilis, the 1943 survey showed an appreciable decrease in the percentage of falsely doubtful and positive reactions in serums of normal nonsyphilitic individuals. The percentage of these reactions with various complement fixation tests dropped from between 1.0 and 10.0 percent in 1936 to between 0.7 and 0.8 percent in 1943. Some improvement has occurred in the various flocculation tests, which varied from 1.0 to 40.0 percent in 1936 to between 0.8 and 16.8 percent in 1943.

Cerebrospinal fluids are much less likely to yield these reactions. The author believes this indicates that the reagin-like substance that may occur in the serums of normal nonsyphilitic individuals yielding falsely doubtful and positive reactions does not occur in the cerebrospinal fluids of normal individuals.

Several diseases are known to cause falsely doubtful and positive reactions, which the author believes is due to an increase of the natural group of spirochetal antibody in the nature of an anamnestic reaction. The author classifies the diseases and conditions known or suspected of causing biologic falsely doubtful and doubtful reactions into three groups, of which a variable incidence is seen in yaws; pinta, leprosy, malaria, vaccinia and vaccinoid, infectious mononucleosis, and virus pneu-



monia; an unknown incidence is found in febrile diseases, upper respiratory tract infections, active tuberculosis, septicemia, subacute bacterial endocarditis, acute lupus erythematosus, relapsing fever, rat-bite fever, Weil's disease, typhus fever, and trypanosomiasis; the group in which the evidence is not conclusive includes rheumatic fever, glanders, chancroid (buboes), Vincent's infections, Rocky Mountain spotted fever, lymphogranuloma venereum, leishmaniasis, leukemia, pellagra, psoriasis, coronary thrombosis, diabetes mellitus, eclampsia, lead poisoning, acute alcoholism, ether anesthesia, sulfonamide therapy, and serum therapy.

A table is given summarizing the doubtful and positive reactions reported by author-serologists in the series reviewed as indicative of what may be expected under optimum conditions. This shows an incidence for all cases of syphilis varying from 77.6 to 90.9 percent. Through consideration of the falsely doubtful and positive results an evaluation of the "serologic indices" shows a variance of from 66.5 percent for the Eagle microflocculation test to 84.5 percent for the Mazzini flocculation test.

The author, in collaboration with Brown, is conducting investigations whereby it may be possible to remove certain lipoids with which the nonspecific reagin reacts without reducing the sensitivity of the antigen in relation to the syphilis-reagin.

The entire responsibility of the diagnosis of syphilis should not be placed on the laboratory findings. Serologic tests alone are insufficient in the differentiation between truly and falsely doubtful and positive reactions. The difficulty in the interpretation and management of presumably nonspecific reaction is in relation to the clinical skill and experience of the physician. There is no substitute for thorough clinical examinations.

In cases where the reactions are persistently positive it is advisable to make a tentative diagnosis of syphilis and institute treatment.

A list of 42 references is appended.

In the discussion, Mahoney points out the importance the serologic test has al-

ways played in regard to the diagnosis of syphilis, and suggests a careful scrutiny of all factors involved, especially in the absence of clinical and historical confirmations, before making a diagnosis of syphilis.

**On the persistence of falsely positive serologic tests for syphilis in nonsyphilitic infections.** Albert E. Taussig. J. Lab. & Clin. Med., St. Louis, 29: 473-477, May 1944.

The author discusses the occurrence of positive serologic tests for syphilis in the blood of nonsyphilitic individuals, and reports 4 supportive cases. One case proved to have malaria, the second rat-bite fever, the third cellulitis, and the fourth pneumonia. The malaria patient gave positive Kahn, Wassermann and Kline tests, but after 1½ months' observation the serologic tests were negative and remained so. Of 154 known nonsyphilitic malaria patients seen at the Jewish Hospital and the City Hospital, the author together with Orgel has found 22 percent with positive Kahn and Wassermann tests. All were negative 15 days after defervescence.

The following suggestions are offered to avoid error in diagnosis in patients who show no other evidence of syphilis than a repeatedly positive Kahn and/or Wassermann reaction: (1) In patients who have had a recent acute infection, repeat the Wassermann and a precipitation test in 1 or 2 months. If the test is still positive syphilis is indicated. (2) If a history of recent infection is not obtained, the patient may be a member of a group who give false positive reactions which fluctuate from week to week and from month to month, and weekly tests if not constantly positive may reveal the patient as not syphilitic. (3) A spinal fluid test may aid in diagnosis. (4) Kahn's verification test may aid in doubtful cases, although as yet its results must be interpreted with reserve. (5) Serums positive with the less sensitive technics, such as the Wassermann test, but negative with Kahn or Kline tests are probably not syphilitic.

The author makes the plea not to inaugurate treatment in a patient without other evidence of syphilis than a positive

serologic test until further observation has made it clear that the reaction actually is due to syphilis.

**The evaluation of doubtfully positive serologic reactions.** (Die Bewertung zweifelhaft positiver serologischer Reaktionen.) H. Hüllstrung. *Med. Klin., Berlin*, pp. 1084-1087, 1942. *Abs. Zentralbl. f. Bakt., Jena*, 144: 266, 1944.

The author points out that the practicing physician should be aware of the non-syphilitic diseases which may give positive serologic reactions for syphilis, e.g., yaws, relapsing fever, trypanosomiasis, the nodular form of leprosy, endocarditis lenta, typhus, ankylostomiasis, malaria, scarlet fever, measles, epidemic parotitis, monocytic angina, and probably acute febrile diseases of the lungs. Treatment with certain drugs, e.g., atophan, atophanyl, sulfonamides, and with diphtheria serum may also result in false positive reactions. Among his material covering the period from 1933 to 1942 the author found only 0.65 percent of pseudo-positive syphilis reactions. He states that at the present time the Meinicke clarification reaction (M.C.R.II) is the most specific serologic test for syphilis. Poehlmann found only 8 nonspecific reactions among 1,245 serologic tests by means of the Meinicke clarification reaction.

**The development of the Pallida reaction and its applicability.** (Die Entwicklung der Pallidareaktion und ihre Brauchbarkeit.) Gerda Remmers. *Ztschr. f. Immunitätsforsch. u. exper. Therap., Jena*, 101: 40-57, 1942. *Abs. Zentralbl. f. Bakt., Jena*, 143: 351, 1943.

The author compared the results of the Gaetgens' Pallida reaction (P.R.) with those of the Wassermann (W.R.), the Meinicke clarification (M.Kl.R.), and the citochol reaction (C.R.) of Sachs-Witebsky on a total of 14,303 serum samples. Of this number 1,017 were found to be positive. In the positive specimens the P.R. was more strongly positive than the W.R. in 54 percent, equally positive in 32.8 percent, and less strongly positive in 13.2 percent. The W.R. was negative in 94 of the 1,017 definite cases of syphilis whereas

the P.R. was negative in only 14; the C.R. was negative in 39 cases, the M.Kl.R. in only 11 cases. Nonspecific P.R.s were obtained in 2.2 percent of cases. The P.R. is superior to the W.R. particularly in cases of latent syphilis and in central nervous system syphilis. The P.R. and the M.Kl.R. are both excellent tests, the latter being superior only in congenital syphilis. The P.R. is of value in the diagnosis of multiple sclerosis in that it always gives a negative reaction. In the examination of the spinal fluid the P.R. takes an intermediate position between the W.R. and the M.Kl.R., the latter being the most sensitive test. It is recommended that all three tests be used simultaneously.

**Unusual behavior of syphilitic reagin following intensive treatment of early syphilis.** Arthur G. Schoch and Lee J. Alexander. *Am. J. Syph., Gonorr. & Ven. Dis., St. Louis*, 28: 305-309, May 1944.

The authors report a case which they consider unique in their experience. In this patient the Kolmer, Kahn, and Kline tests indicated a very low syphilitic reagin titer in the blood serum approximately a year following completion of treatment of early syphilis. However, at this point a quantitative Kolmer done on the same serum with Difco antigen yielded a positive reaction in excess of 1,000 units of reagin. They attribute the marked discrepancy between the Kolmer-Wassermann test done with Difco antigen and that done with their standard antigen to the presence of the multiple lung abscesses of 6 months' duration.

A 16-year-old Negro female was given intensive arsenotherapy for secondary syphilis. She received a total of 1,200 mg. mapharsen over a period of less than 8 weeks. For the first 6 months the quantitative Kolmer, quantitative Kline and standard Kahn tests showed a favorable decline in the serologic titer. At this time the patient was discovered to have non-tuberculous multiple lung abscesses.

From the sixth to the fourteenth month following intensive arsenotherapy the quantitative Kline test fluctuated over and beyond a normal laboratory fluctuation.



The complement fixation reaction, using two different types of antigen at one particular point, indicated a discrepancy of a thousand units of reagin. The standard Kahn qualitative test fluctuated from positive to negative to positive again. At a time when a standard Kolmer and two flocculation tests indicated a low reagin content, the Difco antigen indicated a reagin content of a little more than a thousand Kolmer units.

Repeated testing of this patient's blood serum indicated that the paradoxical results were not the result of technical error, but rather of the peculiar association of syphilitic reagin coupled with nonspecific reagin associated with prolonged febrile disease. Little is known about the mechanism involved in producing false positive serologic tests by the presence of reagin-like substance in the blood of patients with febrile diseases.

**Granuloma inguinale as a cause of arthritis and osteomyelitis: Report of a case.** Roger B. Scott, John Lyford, III, and Robert W. Johnson, Jr. *Bull. Johns Hopkins Hosp.*, Baltimore, 74: 213-217, Mar. 1944.

A 20-year-old Negro woman was admitted to Johns Hopkins Hospital Aug. 11, 1943, complaining of a genital sore and abdominal pain. Seven weeks before admission she developed a small vulvar ulcer which grew progressively worse, with a watery vaginal discharge and tender swelling in both groins and low abdominal pain. Oral sulfonamide treatment gave no relief. She had persistently high temperature (101.4° on admission) and lost 15 pounds in weight. Pain and swelling were seen in the elbows, knees, wrists, and toe. The blood serologic tests for syphilis, the Frei test, the Ito-Reenstierna test and the lymphogranuloma venereum complement fixation test on blood serum were negative.

Microscopic sections of tissue from the bone, joint, and genital lesions showed Donovan bodies in large macrophages, together with massive collections of plasma cells in the exudate. Continuous tissue cultures were made of material from the lesions (arthritis and osteomyelitis), and in

these cultures the organism grew for several weeks. Typical Donovan bodies were seen in the macrophages and in large mesenchyme cells, and were also seen in the medium between the tissue cells as small colonies not much larger than the cells. Cultures on ordinary media of material from the lesions were sterile.

On Nov. 4 because of the persistent ulcer, the left third toe was amputated. Microscopic examination revealed osteomyelitis of the proximal phalanx and chronic inflammation of the subcutaneous tissues. In both the bone and soft tissues there were many plasma cells and scattered large macrophages filled with Donovan bodies. The joint manifestations subsided gradually and the joints assumed the characteristic appearance of a "rheumatoid arthritis."

Treatment consisting of daily administration of 3 to 6 gm. sulfadiazine, orally, and 4 injections of fuadin had no effect on the lesions. Despite frequent transfusions of whole blood the hemoglobin level ranged from 33 to 60 percent, and the white blood cell count varied from 13,000 to 27,000.

The authors are making further studies on similar cases which will be reported at a later date.

**Ocular manifestations of syphilis.** Lyne Gamble. *Mississippi Doctor*, Booneville, 21: 314-315, Apr. 1944.

Due to certain pathologic changes which take place in the entire body of an individual infected with *Treponema pallidum*, ocular manifestations of syphilis constitute from 6 to 10 percent of all cases of blindness, and about 2 percent of all eye diseases are caused by syphilis. The organisms act as a slow irritant and the tissues accumulate lymphocytes and plasma cells. The new tissue is highly vascularized and perivascular round cell infiltration is a prominent feature; later granuloma formation occurs with necrosis and healing by fibrosis.

The ocular manifestations of syphilis follow a natural course. In the primary stage there is a general systemic infection. The secondary stage manifests itself by paresis of the oculomotor muscles and iritis. The tertiary stage is characterized by optic

atrophy and oculoneural changes, or uveitis and keratitis may result.

The orbit may be involved by a chronic periostitis in adults and in children with congenital syphilis, and tertiary syphilis sometimes causes an increased thickness of the orbital bones resulting in a gradual contraction of the orbital cavity, with consequent exophthalmos and pressure on the orbital nerves producing paralysis of the ocular muscles and neuralgia.

Chancre of the lids is not infrequently seen and gummas of the lids usually occur in the form of indolent ulcers.

Chancre of the conjunctiva begins as a papular swelling, becoming ulcerated at its apex. A simple conjunctivitis frequently occurs early in the secondary stage. Granular syphilitic conjunctivitis appears as a diffuse rose-red jellylike thickening of the tarsal conjunctiva, while syphilitic scleroconjunctivitis is limited to the bulbar conjunctiva and produces a diffuse rose-red thickening of the conjunctival and subconjunctival tissues. Syphilitic papules and gummas of the conjunctiva are rare but do occur.

Syphilis usually involves the sclera, and sometimes a diffuse scleritis complicates interstitial keratitis. Interstitial keratitis is the most common ocular involvement and the majority of the cases are those of congenital syphilis.

Acute syphilitic corneal abscess is sometimes seen in acquired syphilis, while iritis is usually a manifestation of the secondary stage, either acquired or congenital. Involvement of the ciliary body by a gumma is uncommon.

Involvement of the choroid is more common in congenital than in acquired syphilis, especially the type described by Forster. The pepper and salt fundus is a frequent manifestation of congenital syphilis. The fundus is covered with numerous yellowish spots and numerous spots of fundus segment. In retinitis (neuroretinitis or chorioretinitis) the changes are due largely to an obstructive endarteritis. Diffuse neuroretinitis is common in the secondary stage of syphilis. Neuroretinitis, neuritis, or retrobulbar neuritis may occur, depending on the point of involvement of the infec-

tion. Syphilitic optic neuritis occurs usually with acute syphilitic meningitis.

Primary optic atrophy occurs in 6 to 7 percent of tabes and about 10 percent of paresis. It is considered by some to be a retrobulbar peripheral and interstitial neuritis, is always bilateral and progresses into blindness in less than 10 years.

Central nervous system syphilis is frequently the cause of paralysis of the ocular muscles. The exact location of the lesion which is responsible for the Argyll-Robertson pupil is unknown. This miotic pupil which reacts in accommodation but not to light is found in 70 per cent of tabetics.

**Use of ejaculation fluid in a final test for a cure in gonorrhea.** Leo Dub. Urol. & Cutan. Rev., St. Louis, 48: 181-183, Apr. 1944.

With the increase in the efficiency of culture methods, the dangerous former methods of obtaining specimens for tests of cure of gonorrhea are no longer necessary. Urine sediments and secretions from the urethral mucosa, the prostate, and the seminal vesicles are now used. The usual method of stroking the prostate in order to get specimens for culture tests is not an adequate stimulus to procure prostatic secretion as part of the spermatic fluid, but during erection all the glands of the urogenital tract become hyperactive and their secretions appear in the urethra. Anatomic and physiologic considerations have caused the author to use the ejaculation fluid as a specimen for the final culture test for a cure in gonorrhea.

The average patient will experience neither mental nor bodily harm from performing the act at the direction of his physician. The penis is cleansed and a condom drawn over it. The patient then produces ejaculation by means of masturbation. Immediately after ejaculation, swabs are inserted into the meatus and prepared for culture study. The patient then voids, the sediments of urine thus being mixed with ejaculation fluid. If only one specimen is to be used for culture the urine should be used.

Spreads are prepared from the ejaculation fluid in the condom, gram-stained and



examined for gonococci and pathologic contents.

**Clinical observations in yaws.** (Observaciones clinicas de buba.) Ildemaro Lovera. Rev. san. y as. soc., Caracas, 8: 1073-1092, Oct. 1943.

Although yaws is characterized by various stages, it is difficult to say where one stage terminates and the other begins; the lesions of one stage may coexist with those of another; one stage may be absolutely lacking.

Among the cases studied by the author 1,309 patients did not remember having had a primary lesion and 849 definitely denied ever having had an initial lesion.

The author describes the lessons of the primary, secondary and tertiary stages of the disease.

After the treponeme has penetrated the skin, a period of from 2 to 8 weeks elapses before the primary lesion appears. During this incubation period the symptoms are malaise, slight fever, and bone and joint pains. The primary lesion is a pinhead sized, moist papule on a slightly infiltrated red zone and is sometimes pruriginous. It bleeds easily and is painful, particularly when located on the lower extremities. In the author's experience primary lesions may occur anywhere on the body, the great majority being observed on the dorsum of the foot and the legs, comparatively few on the genitals. This lesion lasts for approximately 2 or 3 months, and then becomes covered with a thick crust. If this crust is removed the underlying skin is seen to be shiny, atrophic, hyperchromic, and slightly erythematous. The scar which is formed is completely pigmented or has a pigmented border.

The secondary stage is initiated with symptoms such as malaise, fever, bone and joint pains and is characterized by generalized papular skin eruption. The lesions, however, may be very large, giving the impression of multiple primary lesions. Lesions at the labial commissures may resemble perlèche. Generalized lymphadenopathy and osteitis, particularly of the extremities, also occur. The duration of these lesions is usually from 3 to 6 months,

but sometimes verrucous lesions persist 2 years or longer; they may disappear and then reappear after 5 to 6 months. Such periodic recurrences may take place annually during the first 5 or 6 years of the disease. For this reason all untreated patients must be considered infectious for others during the first 5 or 6 years of the disease.

The transition between the secondary and tertiary periods is not clear-cut since tertiary lesions, particularly hyperkeratotic plantar or palmar lesions, osteitis, and synovitis, may coexist with secondary lesions. Tertiary lesions may occur for as long as decades after the primary infection. The author has seen bilateral plantar hyperkeratotic lesions in a man 95 years of age.

Among 3,646 patients the author observed the following types of tertiary lesions: hyperkeratoses in 2,644, ulcerating gummas in 489, synovitis and bursitis in 201, rheumatism due to yaws in 185, corneal lesions in 57, osteitis and periostitis in 47, extensive mutilating lesions of the fingers or toes in 22, and rhinopharyngitis in 1.

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## TREATMENT

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### Treatment of 500 cases of sulfonamide-resistant gonorrhea with penicillin.

Robert L. Daily, Joseph B. Weynert and Jacob Saltaman. M. Bull. N. African Theater of Operations, 1: 21-22, May 1944.

Penicillin has been available for the treatment of gonorrhea at the Fifth Army Venereal Disease and Diagnostic Center since Feb. 17, 1944. Due to the limited supply its use was restricted to patients whose gonorrhea was proved to be resistant to sulfonamides after one or more complete courses of treatment. In each course, a minimum of 23 gm. of sulfonamide has been considered a satisfactory trial. Five hundred consecutive cases have been treated with penicillin.

The standard dosage of penicillin was

carefully controlled. A course consisted of 100,000 Oxford units, injected intramuscularly, in 5 doses of 20,000 units each, at 3-hour intervals. To avoid deterioration of the active principle of the penicillin solution, it was at all times refrigerated to a temperature of 10° C. or lower. The preparation as issued was diluted with chilled normal saline to a potency of 5,000 Oxford units per cubic centimeter. This diluted solution was not warmed prior to injection. The unused portion was always returned to the refrigerator. Every 24 hours a fresh dilution was prepared in the exact amount required for the following day's use. Patients received 4 cc. (containing 20,000 Oxford units) intramuscularly in the deltoid regions of alternate arms at 3-hour intervals until a total of 5 doses had been given. Other than transitory pain at the site of injection, no untoward reactions were observed.

Additional courses of penicillin were administered in 24 cases where there continued to be a purulent discharge after the course of treatment. Of these 24 cases, 18 were cured following a second course, and 5 following a third course. In 1 case a purulent discharge remained after the third course of treatment. In this series, therefore, 95.2 percent were cured within 24 hours after the first injection of penicillin. Six patients (1.2 percent) were apparently cured but relapsed within 1 week, showing positive spread after the first treatment.

**The treatment of gonorrheal urethritis with sulfonamides and penicillin combined.** Harry C. Oard, E. V. Jordan, Meyer Nimaroff and William J. Phelan. J.A.M.A., Chicago, 123: 323-325, June 3, 1944.

When penicillin became available at the U. S. Naval Hospital, Bainbridge, Md., in October 1943, a large number of patients with sulfonamide resistant urethritis were under treatment. Penicillin sodium was given in a dosage of 160,000 Oxford units (O.u.) at the rate of 10,000 O.u. every 3 hours, with rapid, efficacious results, clinical and bacteriologic cure resulting within

24 hours. The dosage was decreased and 73 sulfonamide resistant patients received 50,000 O.u., with 1 treatment failure. After Rammelkamp and Keefer suggested a combination of a sulfonamide compound with penicillin, the authors felt that it was desirable to investigate the effect of a combination of sulfathiazole with small doses of penicillin, and 232 patients were so treated. (Since this report, the authors have added 71 cases.)

The method of treatment was as follows: On the first day 8 gm. of sulfathiazole was given orally in 4 divided doses; on the second day 4 gm. in divided doses with the concomitant administration of 50,000 O.u. of penicillin at the rate of 10,000 units every 3 hours into the muscle. Among the group consisting of 27 white recruits found to have gonorrhea and 43 white men with acute untreated disease, 8.57 percent failed of cure, and among 114 Negro recruits found to have gonorrhea and 48 Negroes with acute untreated disease, 2.47 percent failed, giving a failure in 4.31 percent out of the 232 cases treated. Gonorrheal urethritis of the Negro is shown, therefore, to be more responsive to treatment with penicillin and with penicillin and sulfathiazole combined than it is in the white race.

The authors believe that sulfathiazole and penicillin enhance the effect of each other against *Neisseria gonorrhoeae*, and their combined use in moderate amounts is a safe, rapid, efficient and economical method of treating gonorrheal urethritis.

**Three hundred chemoresistant cases of gonorrhea treated by hyperpyrexia and chemotherapy.** A. J. Gewirtz and Morris Polsky. Urol. & Cutan. Rev., St. Louis, 48: 178-181, Apr. 1944.

A consecutive series of 300 soldiers who were given combined sulfonamide and fever therapy for chemoresistant gonorrhea is reported. All patients had had at least 2 courses of chemotherapy consisting of 20 gm. of either sulfathiazole or sulfadiazine. No case was of less than 20 days' duration, while in several patients the infection had been present for 3 or more years. The present treatment consisted of 8.0 gm. of



sulfathiazole given in divided doses in the 8-hour period preceding pyretotherapy, followed by 7 hours of temperature sustained at 106° F.

One treatment cured 266 (89 percent) of the 300 treated. A second treatment cured an additional 7 percent, making a total of 287 cures, or 96 percent. If the 4 cases who refused the second treatment are excluded, the total cures aggregate 287 out of 296, or 97 percent. No relapses have been observed.

Of the 9 cases not cured by the second treatment, 8 were cured by means of local conservative measures, and 1 by a 5-day course of sulfathiazole and 3 fever treatments of 3 hours at 106° F. The psychiatric appraisal of the relatively small group of soldiers who persistently refuse to accept fever therapy revealed that the majority had either mental deficiency, severe psychoneurosis, or constitutional psychopathic states.

A mild herpes labialis was encountered in about 80 percent of the patients, 9 patients had corneal ulcerations following the fever therapy, approximately 15 percent complained of nausea and vomiting, 1 patient developed jaundice, and 1 patient developed a bilateral Bell's palsy 72 hours after fever therapy. One death occurred in 675 consecutive fever treatments (0.14 percent).

**The laboratory control of penicillin treatment.** Lawrence P. Garrod. *Brit. M. J.*, London, **No. 4345**: 528-530, Apr. 15, 1944.

The clinical use of penicillin requires a great deal of laboratory work, and where many cases are being treated it is advisable that a laboratory worker devote full time to these duties. The work falls into three categories: the preparation of solutions, bacteriologic diagnosis, and observation of the results of treatment by various *in vitro* tests.

The methods of preparing penicillin for clinical use are described in M.R.C. Memorandum, which is to be published in the near future. The drug comes in the form of powder or tablets, from which solutions of various strengths and diluted powders

or creams are made. As the drug is very labile, adverse conditions will cause loss of activity.

Penicillin is not an antiseptic; therefore it can easily become a vehicle of cross-infection. For this reason, it is advisable for each patient under local treatment to have his own bottle of solution. Solutions and creams should be kept in the refrigerator before and during use.

As penicillin is effective only against certain bacteria, it is necessary that the nature of the infection be known before treatment is begun. An accurate method is to isolate the responsible pathogen in pure culture and inoculate broth containing various low concentrations of penicillin to determine the least which will inhibit growth. A more rapid method which has proved satisfactory for most purposes and which furnishes both a species and a sensitivity diagnosis from one primary culture is Fleming's agar cup method.

The author gives suggested examinations to check the results of treatment and methods of estimating the penicillin content of the exudates and of the blood. His aim is to present a picture of the nature and volume of work necessary in the laboratory if penicillin treatment is to be directed intelligently and efficiently.

**Experiences in the systemic administration of penicillin.** H. R. Morgan, Ronald V. Christie and I. A. Roxburgh. *Brit. M. J.*, London, **No. 4345**: 515-516, Apr. 15, 1944.

The complications which may arise when penicillin is administered by intramuscular injection or by continuous intravenous and intramuscular drip are discussed. Each method has its advantages and disadvantages for particular cases.

In the continuous intravenous drip injection method of administration of penicillin, which was carried out on 26 patients, 30,000 units of sodium penicillin were dissolved in 1 pint of fluid and injected in 6 hours in adults. The dose of penicillin was reduced in younger patients, and subsequent dosage was controlled by blood titer estimations. The fluid intake was regu-

lated according to the patient's needs. Penicillin was usually dissolved in 4 percent dextrose in 0.18 percent saline, but was sometimes added to blood for injection. Usually a cannula was inserted into the vein, but a needle was used if the treatment was short. The advantages of this method were continuous maintenance of adequate blood titer and combination with parenteral fluid administration. Its disadvantages were the frequent and painful thrombophlebitis (probably due to the impurity of the penicillin) which occurred in 13 of these patients and the results of the treatment on the veins for future occasions.

The intermittent intramuscular injection was used on 12 patients. The standard adult dose was 15,000 units every 3 hours. The reactions, both general and local, varied from case to case. On the whole, the patients tolerated the later batches of penicillin better, which seemed to be due to the degree of impurity of the preparation, the condition of the patient, and the volume of individual injections. This method has the advantage of being simple, although it causes pain and disturbance of the patient and a rise and fall in blood titer.

The drip into the bone marrow was administered to 5 patients, including 2 six-week-old infants in whom the site of entry of the drug was the tibia. Dextrose-saline was employed in all of the cases. Samples of bone marrow from sternum and tibia were examined before and after injection, and showed no changes which could be attributed to penicillin. Although the value of this method is doubtful, the results were encouraging enough to warrant further trial.

The continuous intramuscular drip method of administration was attempted in 6 patients, aged 12 to 19 years. The same dose of penicillin used in the intravenous route was employed, with the dextrose-saline medium in all of the cases. Two pints of fluid every 24 hours were given with an ordinary intramuscular needle with an improvised wire frame for supporting it in position. The site of entry was the thigh. In some cases local abscesses

formed around the site of entry and culture of the pus showed a growth of coliform bacilli. The method is almost totally without pain and the swelling of the thigh was slight provided the rate of drip was kept constant. Investigations are now being carried out with regard to improvements of the technic with encouraging results. The advantages of this method are (1) continuous maintenance of adequate blood titer, (2) comparative freedom from pain, and (3) availability of numerous sites for injection. It has the disadvantage of a tendency to local infection and abscess formation at the site of entry which occurred in 2 of these cases and the possibility of having to restrict total fluid intake.

**The use of penicillin in the Navy.** Joseph S. Barr. *J. Bone & Joint Surg., Boston*, 26: 380-386, Apr. 1944.

In July 1943 sufficient quantities of penicillin were made available to the Navy to permit supplying 10 naval hospitals with limited amounts of the drug, with the addition of other hospitals within the next few months.

Prior to Jan. 1, 1944 a total of 1,750 cases of sulfonamide resistant gonorrhea were treated with penicillin. Of these, 1,701 (97.2 percent) were cured with one course of treatment, while 31 additional cases were cured by retreatment, making a total percentage of successful cures of 99. The criteria for cure included complete subsidence of all clinical signs and symptoms along with bacteriologic sterilization of the involved genitourinary tract. The intramuscular and intravenous methods of administration were the most commonly used.

Preliminary reports by Mahoney indicate that in primary syphilis, penicillin therapy causes rapid reversal of the serologic tests and disappearance of the local lesion. A series of cases is now being studied at the Naval Hospital, Bethesda, Md. Although the preliminary reports are very promising, the use of penicillin in the treatment of syphilis has not been authorized for general use in the Navy.



Effective Feb. 1, 1944, penicillin was made available to all ships and shore stations in the Navy in sufficient quantities to fill reasonable needs.

**The effects of sulfonamide drugs on the blood.** Roy R. Kracke. *Am. J. Clin. Path.*, Baltimore, 14: 191-199, Apr. 1944.

The toxic effects in occasional patients due to the concentration of a sulfonamide in circulating blood and in the marrow are discussed under the four headings: the production of cyanosis, effect on the red cells, on the white cells, and on the blood platelets.

From a review of the observations by various investigators it is apparent that the cause of cyanosis is not settled and the condition is now considered of little significance. There appears to be no interference with oxygen carrying capacity and no ill after-effects.

Acute hemolytic anemia is characterized by quickly increasing pallor, nearly always fever, and a rapid decrease in the red cells and hemoglobin. At the same time there is evidence of increased red cell destruction, with reticulocytosis, increased icterus index, urobilinogen, and perhaps clinical jaundice. On the appearance of such signs, the blood picture should always be investigated and treatment discontinued. The blood values should be restored by transfusions, the urine kept alkaline, and kidney damage watched for.

Leukopenia does not occur so frequently as does acute hemolytic anemia, but when it does occur it presents a far more serious problem. Agranulocytosis follows the administration of sulfonamides only after they have been given for a considerable time. Its treatment should include prompt cessation of the offending drug, repeated transfusions, a liberal fluid intake, intensive treatment with liver extract, intramuscularly, and the use of pentnucleotide. Periods of leukopenia may develop frequently in patients who are taking sulfonamides, but when the leukopenic state does not reach complete agranulocytosis recovery is the rule.

As might be expected from drugs that are known to destroy cells and suppress leukopoiesis they are also capable of producing marked thrombocytopenia with resulting hemorrhages and often death of the patient. The author has observed two patients with this complication during the past year. In an occasional patient the granulocytes may show an alarming degree of immaturity, so that the condition may be properly labeled as a leukemoid reaction. It is observed sometimes in a patient who is showing clinical improvement.

The author has observed that a great many patients with leukemia that he has seen in recent years give a history of administration of sulfonamide drugs apparently prior to the development of the leukemia.

There should be effective legislation to prevent the sale of the sulfonamides to the public, and a program of education to advise the public of the dangers of their indiscriminate use.

**The effect of sulfadiazine on the coordination and reaction time of young men.** Alison H. Price and John C. Pedulla. *J. A. M. A.*, Chicago, 125: 105-107, May 13, 1944.

In order to study the coordination and reaction time of individuals treated with sulfadiazine, tests were made on 134 medical students ranging in age from 22 to 34 years. Ninety of the students were given sulfadiazine and 44 served as controls.

An initial dose of 2 gm. sulfadiazine by mouth, followed by 1 gm. every 4 hours, was given to a total dosage of 19 gm. A special apparatus which simulated actual working conditions was used to measure the coordination and reaction time in the persons who were given sulfadiazine and in those used as controls. Eye-hand coordination and reaction times were automatically recorded by an electric clock. Tests were made before and during the administration, and 7 days after the drug was discontinued. No significant difference between the controls and those subjects given sulfadiazine was found.

**Relative toxicity of sulfamerazine and sulfadiazine.** Harry F. Dowling, Edith Dumoff-Stanley, Mark H. Lepper and Lewis K. Sweet. *J. A. M. A.*, Chicago, **125**: 103-105, May 13, 1944.

A study was made of the toxic reactions of 900 patients treated with sulfadiazine and 428 with sulfamerazine at the Gallinger Municipal Hospital, Washington, D. C., and patients from private practice of one of the authors.

Toxic reactions occurred in 10.0 percent of 428 patients to whom sulfamerazine was administered, compared with 8.1 percent of 900 patients receiving sulfadiazine.

There was no significant difference between the incidence of any individual toxic reaction in the two groups, with the exception that renal calculi were more frequent following the administration of sulfamerazine. Drug fever (with or without dermatitis and conjunctivitis) was also more frequent following sulfamerazine, although the difference was not statistically significant. When the patients were compared according to dosage or according to the average free sulfonamide levels reached in the blood, these toxic reactions more frequently followed the administration of sulfamerazine than the administration of sulfadiazine.

Drug fever occurred more often during a second course of sulfamerazine than during a second course of sulfadiazine.

Sulfadiazine is the drug of choice for systemic sulfonamide therapy at the present time.

#### **The oral use of sulfathiazole in the prevention of gonorrhea and chancroid.**

Ernest E. Keet, Jr. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, **28**: 315-319, May 1944.

The prophylactic use of a single dose of 1 gm. sulfathiazole given orally within 12 hours after sexual exposure was studied in 1,802 men attached to the U. S. Naval Armed Guard Center, Brooklyn, N. Y. The control group consisted of 503 similar exposures where no sulfathiazole prophylaxis was used.

In the group receiving sulfathiazole, gonorrhea occurred 15 times and syphilis once,

an incidence of 1 in 120 exposures (reports were usually returned prior to the end of the incubation period for syphilis), and no cases of chancroid were found. In the control group, gonorrhea occurred 13 times (an incidence of 1 in 39 exposures) and chancroid 5 times.

Except for skin sensitization in some of the men receiving two or more prophylactic doses, no important toxic manifestations occurred.

The administration of 1 gm. prophylactic dose of sulfathiazole did not affect the length of the incubation period nor therapeutic response to sulfathiazole in those cases which developed gonorrhea.

Although the incidence of gonorrhea was somewhat higher with this dosage schedule than has been previously reported with 4 or more grams, the smaller dose was used as it was felt that it was more applicable to the Armed Forces because of decreased likelihood of producing transitory ocular or mental impairment. The author suggests, however, that an attempt be made to determine the optimal prophylactic dose of sulfathiazole which will produce no untoward toxic effects.

#### **Recent cases illustrating dangers of the sulfa drugs.** John K. Ormond and Russell B. Roth. *J. Urol.*, Baltimore, **51**: 92-96, Jan. 1944.

The present trend in the use of sulfonamides is to go beyond indicated uses for them; soldiers carry tablets with them into combat service and there seems to be a widespread use as prophylaxis against gonorrhea. The dangerous potentialities in their use should be realized and physicians should be alert for the detection and prevention of untoward results for their use. The authors review three recent cases illustrating the nature of the dangers involved.

A Negro woman with diabetic acidosis and signs and symptoms of bronchopneumonia was given sulfadiazine for the latter. The diabetes resisted all efforts at control; by the third day urinary output had dropped sharply and the number of acetyl-sulfadiazine crystals in her urine had increased. She died on the seventh hospital



day. This case illustrates urinary tract obstruction due to precipitation of acetyl-sulfonamide crystals, and the necessity of overcoming the diabetic acidosis when using a sulfonamide.

A 52-year-old man entered the hospital for a transurethral resection for a prostatic obstruction. During preoperative catheter drainage he was given sulfathiazole, and, following resection of median lobe, sulfathiazole was resumed because of an elevation of temperature. He became disoriented, and a rash appeared over the entire body. Anuria developed, and the patient died in uremic coma. Evidence suggested focal necroses scattered throughout the kidneys, spleen, liver and skin, attributable wholly to sulfathiazole toxicity.

The third case illustrated sensitivity to sulfathiazole, the patient developing severe reactions each of the 3 times the drug was tried, the second time with symptoms suggesting an acute condition in the abdomen, and the third time with anuria.

The authors mention other cases which also illustrate the three types of renal damage which may result from sulfonamides: the obstruction, due to crystals of the acetylated drug; the widespread focal necrotic type in which the kidney is only one of many organs involved; acute toxic nephritis in which anuria and uremia are the clinically striking pictures.

**Skin pigmentation following sulfonamide therapy: Report of a case.** Frank E. Fox and Alfred A. Schiller. U. S. Nav. M. Bull., Washington, 42: 923-928, Apr. 1944.

A case of exfoliative dermatitis and associated reaction simulating a serum reaction followed by pronounced pigmentation of the skin is reported. A 25-year-old seaman was admitted to the hospital with a diagnosis of measles coincident with a gonorrheal urethritis. He had been receiving 1 gm. sulfathiazole every 4 hours during a 10-day period for a total of 60 gm.

Examination disclosed a generalized morbilliform eruption which was considered to result from sulfathiazole sensitivity,

and gonococci in the urethral discharge. The blood Kahn test was negative.

After a 10-day rest from the sulfonamides, during which time the skin eruption disappeared, the patient was given 1 gm. sulfapyridine twice a day for 3 weeks, up to a total of 46 gm. The drug was discontinued because of headache, sore mouth, a generalized scarlatiniform eruption, severe conjunctivitis on the exposed portion of the scleras, and a temperature of 102° F., followed 24 hours later by severe pruritus, dyspnea and generalized edema, a temperature of 104° F. and pulse rate 120. The patient was moderately irrational and disoriented. This condition gradually cleared up under treatment, but marked pigmentation occurred, gradually increasing to a chocolate color. A skin biopsy showed increased melanin deposits. This pigmentation lasted for 2 months and then faded very gradually. Along with the skin exfoliation there was loss of hair on the head and in the axillas and transverse furrowing of the nails of the hands and feet. The patient was discharged to duty 5 months after admission.

The sulfonamides have been found to produce skin eruptions in approximately 5 percent of cases in which the drug is used. Many of these may be prevented by observing the following precautions: (1) A careful family and personal history should be taken; (2) sunlight, sun lamps and X-rays while receiving treatment should be avoided; (3) blood should be examined frequently during treatment; (4) other drugs in conjunction with the sulfonamides should not be given; (5) sulfonamides should not be used for minor infections because of the danger of sensitivity.

**Fever therapy in chemoresistant gonococcus infections: An analysis of 150 consecutive cases.** Gordon M. Perisho. U. S. Nav. M. Bull., Washington, 42: 971-976, Apr. 1944.

Chemotherapy resistant gonococcal infections are a serious problem among Navy personnel, and are a cause of a large number of lost man-hours. With this problem

in mind, the author evaluated the results of fever therapy in 150 cases of chemotherapy resistant gonococcic infections.

The method of fever therapy used was the single long session, at temperatures of from 106° to 106.8° F. for 8 hours. The technic was the same as that described by other fever therapists. Each patient was given sulfadiazine or sulfathiazole for 48 hours before, and 48 hours after fever therapy.

Of the 150 cases treated, at least one 8-hour session of therapeutic fever sustained at a rectal temperature of from 106° to 106.8° F. was obtained in 125 cases. Of these 125 cases, 121 (96.8 percent) were clinically cured, 107 resulting from a single session and 14 from one or more repeat sessions. In this group of patients, no one received more than 3 sessions and no more than 20 hours of fever. Of the 25 patients who failed to complete 8 hours of treatment, 19 (64 percent) were cured sufficiently soon after their fever treatments to conclude that this treatment contributed toward the cure. Of the total number of cases treated, 91.3 percent were cured.

The majority of failures of treatment in this series was attributed to abnormal emotional or hysterical reactions of the patient. However in one case the patient worked in an environment of high temperatures and high humidity, and in another the patient had had several short sessions of fever therapy without benefit. It was believed that the body heat regulating mechanisms had become adapted to high environmental temperatures, rendering them resistant to artificially induced fever.

Four patients, within 18 hours after their fever session, developed a severe acute epididymitis, although this condition was not present before treatment. In all 4 the epididymitis completely subsided within 48 hours, together with all other clinical signs of gonorrhea, and a complete cure resulted. The author believes this complication was of sufficient interest to mention as no previous reports have been noted.

For the present, fever therapy seems to be the best means of rehabilitating chemotherapy resistant cases of gonorrhea.

**Rapid treatment of neurosyphilis with malaria and chemotherapy.** Bernhard Dattner, Evan W. Thomas and Gertrude Wexler. *Am. J. Syph., Gonorr. & Ven. Dis., St. Louis*, 28: 265-285, May 1944.

From Jan. 1, 1939 to June 1, 1943, 419 neurosyphilitic patients were treated with malaria followed by some form of chemotherapy at Bellevue Hospital. The patients were classified according to the type of neurosyphilis as follows: asymptomatic 125, meningovascular 35, general paresis 74, tabes dorsalis 103, taboparesis 34, tabes with optic atrophy 32, congenital 16 including 4 juvenile paresis. Of 424 fever treatment courses (5 were retreated with a different strain of malaria), 148 had malaria followed by routine chemotherapy and 276 had malaria followed by a daily injection of 0.06 gm. mapharsen for 10 days. No previous antisiphilitic treatment had been received by 141 patients. The patients were given the tertian or quartan type of malaria and limited to 8 paroxysms.

Of the 419 patients, 331 were males, 88 females; 353 were white, 57 Negro, 6 Puerto Ricans, 3 Chinese; the youngest patient was 11 years old, the oldest 67 (113 were over 50 years of age). With a few exceptions, all of the patients had positive spinal fluid findings at the time of admission.

No special differences were noted in the results of the two groups treated. However, the patients whose chemotherapy following malaria was limited to a daily injection of 0.06 gm. mapharsen for 10 days gave as good or better results than those who received at least 6 months of routine weekly injections of arsenical drugs or bismuth. Much time can be saved by using the former method and there is the advantage of completing therapy while the patient is still in the hospital. Of the entire series, 10 (2.35 percent) deaths were attributed to malaria. Of 298 treatment courses in both groups where patients were followed from 6 to 48 months after treatment, satisfactory results shown by spinal fluid examinations made over 6 months after completion of treatment were obtained in 85.9 percent. The results are



tabulated according to the type of neurosyphilis and method of treatment used. The highest percentage of unsatisfactory results occurred in patients having advanced general paresis and taboparesis.

Reasons are given for evaluating results on the basis of spinal fluid findings rather than clinical symptoms. Using the spinal fluid findings as a guide, prolonged chemotherapy following malaria is considered unnecessary and unwise.

The case histories of 6 of the authors' cases are given in detail.

**Induction of fever by the intravenous infusion of triple typhoid vaccine in the treatment of syphilis.** Herbert Lawrence. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, 28: 289-304, May 1944.

The literature is reviewed on the various methods of producing fever for the combined fever and chemotherapy method of treatment of syphilis.

The technic employed by the author consisted in the continuous infusion of typhoid vaccine in a saline suspension as described by Solomon and Somkin. The infusion was prepared by adding the selected amount of Army triple typhoid vaccine (1,000 million *B. typhosus* per cubic centimeter; 250 million *B. paratyphosus* A per cubic centimeter; 250 million *B. paratyphosus* B per cubic centimeter) to 1 liter of saline, which was then shaken thoroughly. The solution was administered intravenously at an initial rate of 25 drops per minute; if the chill did not appear within 1½ hours, the rate was increased to 50 drops.

In the treatment of 10 patients among the Army personnel at 147 General Hospital, San Francisco, using the Army triple typhoid vaccine, the initial dose was 10 times the amount recommended by Solomon and Somkin. (Nine of the patients had been immunized against typhoid fever within 20 months, and 1 had had clinical typhoid fever in childhood and had been immunized about 5 years ago.) So far, about 400 hours of fever over 104° F. have been given to these 10 patients without serious complications. In 2, vasomotor collapse did occur but responded readily to treatment. Three of the cases are de-

scribed in detail with accompanying temperature charts.

A sustained fever can be obtained and its height and duration controlled by altering the rate of flow of the suspension. With a single injection of typhoid vaccine, once the vaccine has been administered, it is impossible to alter the course of the fever except for external measures. The single injection and divided dose technics were found unreliable and did not give sustained fevers.

Unlike malaria, the arsenicals can be given at the height of the fever without affecting its course. In these cases 0.06 gm. mapharsen was given at the height of each paroxysm of fever and 0.13 gm. bismuth subsalicylate was given intramuscularly twice weekly on afebrile days.

Some of the advantages of this method of treatment are the comfort of the patient, the feeling of increased body heat and restlessness which patients experience in a cabinet are absent, it is not necessary to administer oxygen, and the mental state of the patient is not affected.

The author concludes that this method is particularly applicable to Army facilities since its only requisites are typhoid vaccine, infusion apparatus and nursing personnel.

#### **Resistance to treatment in early syphilis.**

Frederick Kalz. *Canad. M. A. J.*, Montreal, 50: 534-536, June 1944.

From his observation of cases of early syphilis at the Royal Victoria Hospital, the author believes that most therapeutic failures are due to inadequate dosage of arsenicals during the first month of infection. During the past 5 years, a more intensive routine treatment schedule has been used for the treatment of early syphilis and no instance of resistance has been observed in 200 cases. The plan of treatment used was 0.06 gm. mapharsen given twice weekly for 10 weeks and 2 cc. bismuth subsalicylate once weekly beginning with the ninth week, for 6 weeks; this is followed by a second course of mapharsen twice a week for 10 weeks, again overlapping the bismuth course in the twenty-third and twenty-fourth week. Alternating

and overlapping courses of mapharsen (0.06 gm. once a week) and bismuth subsalicylate (2 cc.) are given until therapy is concluded, the total dosage being 50 to 60 mapharsen and 30 to 40 bismuth subsalicylate.

As treatment for relapsing secondary syphilitic conditions, especially ocular involvement, and other cases where strong arsenical therapy is indicated, an average dose of 0.4 to 0.5 gm. arsphenamine a week has been used routinely.

Three illustrative cases are reported, in which insufficient treatment had been given and where cure was effected after intensive arsphenamine therapy.

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## **PATHOLOGY**

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### **Meningoencephalitis in lymphogranuloma venereum: A report of two cases.**

Chris J. D. Zarafonitis. *New England J. Med.*, Boston, **230**: 567-573, May 11, 1944.

Two cases of meningoencephalitis associated with lymphogranuloma venereum, which may have been the causative factor, are reported. The first case was that of a Negro private who was admitted to the Station Hospital at Indiantown Gap on Oct. 24, 1942, in a delirious condition. He had had an enlarged inguinal lymph node and a urethral discharge since September, following repeated sexual intercourse with the same individual for some weeks. He had been ill since Oct. 10 with severe headaches. After his admission he developed symptoms of meningeal involvement. Late in December, after his transfer to Walter Reed Hospital, lymphogranuloma venereum was first suspected as the causative agent of his condition, and in February, virus from a surgically removed lymph node was identified as lymphogranuloma venereum. Extensive laboratory studies were done while he was in the hospital and he was discharged home on sick leave in June, the final clinical diagnosis being myelomeningoencephalitis with adhesive arachnoiditis secondary to lymphogranuloma venereum.

The second case was that of a Negro

private who was admitted to the Station Hospital at Fort Bragg on July 31, 1940, with swelling and tenderness in the right inguinal region. On Aug. 4, the patient developed frontal and occipital headache and a clinical diagnosis of meningoencephalitis secondary to lymphogranuloma venereum was made.

The diagnosis of lymphogranuloma venereum was based on the clinical history and physical findings, the positive complement fixation tests, the positive Frei tests and in case 1 the isolation of the virus from an inguinal lymph node 5 months after the onset of illness. The virus was identified as lymphogranuloma venereum by its effect in mice, guinea pigs and developing chick embryos, by cross-immunity tests in mice and by complement fixation studies.

Case 1 showed a complete spinal block throughout the 8 months of observation. The author believed that the meningeal involvement early in the course of his illness resulted in subarachnoid block. Extremely high total protein (reaching 3,750 mg. per 100 c.c.) and first-zone colloidal gold curves were also seen in this patient.

In case 1 positive Frei tests were not obtained until the eighth month of illness, and included a positive reaction to an antigen prepared from the virus isolated from the patient. Because of the cross reactions noted in the complement fixation studies, he was also tested against a psittacosis antigen with a negative result.

**Yaws: Report of a case appearing in a white man.** Harold A. Lyons. *U. S. Nav. M. Bull.*, Washington, **42**: 1168-1169, May 1944.

Yaws in the white race is very rare, but an increased incidence is anticipated due to the present war conditions.

The author reports the case of a 36-year-old medical officer on duty on one of the Solomon Islands for 2½ months, in whom the diagnosis of yaws was confirmed following admission to a base hospital. While on duty the patient was in charge of a clinic in which natives were treated for yaws. Six weeks before admission he was bitten on the finger by what was believed to be a centipede. An



acute lymphangitis of the forearm and an epitrochlear lymphadenitis developed which was treated with sulfadiazine. Seventeen days later a lesion appeared at the site of the bite, which gradually enlarged and did not heal. Shortly afterward a maculopapular eruption appeared on the trunk.

Repeated darkfield examination made on board a hospital ship disclosed *Treponema pertenuis*, and the blood Kahn examination was positive. Three intramuscular injections of 0.13 gm. bismuth each were administered.

Physical examination on admission to the base hospital revealed a granulating area overlying the dorsum of the middle phalanx of the fourth finger, 5 mm. in diameter, with moderate surrounding induration; enlarged left epitrochlear and axillary lymph nodes, with evidence of a lymphatic fibrositis on the anterior surface of the forearm; limitation of extension of the left elbow; a visible and palpable periosteal thickening and tenderness of the left radius; a few scattered light brown maculopapular lesions on the trunk.

The patient's course in the hospital was uneventful. On the fourth day of hospitalization an intramuscular injection of 0.36 gm. iodobismutol was given.

The laboratory findings were red blood cells 3,720,000, white blood cells 8,600, hemoglobin 70 percent, polymorphonuclears 44 percent, lymphocytes 56 percent; urinalysis, malarial spread, and chest X-ray were negative.

It was felt that the infection in this case was contracted from the contamination of the injured skin surface, caused by the bite of an insect.

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## LABORATORY RESEARCH

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**Simplified procedures for ascertaining concentration of and bacterial susceptibility to penicillin.** A. R. Thomas, Jr., Max Levine and Guy R. Vitagliano. *Proc. Soc. Exper. Biol. & Med., Utica*, 55: 264-267, Apr. 1944.

Technics requiring only such equipment

and supplies as are already available in any bacteriologic laboratory are presented (1) for developing reference curves and tables which may be used (a) for determination of penicillin concentration of solutions employed therapeutically and (b) for following readily the rate of decrease of penicillin potency, (2) for converting growth inhibition zones (for staphylococci) on seeded agar to probable inhibiting concentrations of penicillin in broth, and (3) which make feasible the tentative allocation of bacteria, in respect to their susceptibility to penicillin, simultaneously with the determination of the types of organisms encountered, in lesions and exudates, within 15 to 18 hours after collection of specimens.

The technic is: To 15 cc. melted nutrient agar cooled to about 45° C. is added 0.05 cc. of a 20-24 hours 37° C. broth culture of the test organism. The contents are then poured into a Petri dish, allowed to harden and placed in a refrigerator until ready for use. To determine the resistance of an organism, 4 mm. loops of one or more concentrations of penicillin, in M/50 phosphate buffer at pH 7.2, are placed on the surface of a seeded agar plate which is then immediately incubated at 37° C., care being taken to keep the plates horizontal to insure that the inhibition zones will be circular. The diameters of the zone of growth-inhibition are measured the following day to the nearest 0.5 mm. A reference curve can be plotted from these diameters of the inhibition zones, and this will be particularly useful for studies on the stability, or rate of destruction of penicillin.

**The relative toxicity of six salts of penicillin.** Henry Welch, Donald C. Grove, Ruth P. Davis and Albert C. Hunter. *Proc. Soc. Exper. Biol. & Med., Utica*, 55: 246-248, Apr. 1944.

Five salts of penicillin, sodium, ammonium, strontium, potassium, and magnesium, prepared from a single master lot were investigated for their acute intravenous toxicity in mice. A sixth salt, a commercial preparation of penicillin calcium, was also included in the study.

Based on milliequivalents of the cation used in the preparation of these salts their relative toxicity was found to be (increasing toxicity): Na, NH<sub>4</sub>, Sr, Ca, Mg and K. The same relative toxicity was found for the acetates of these cations.

The relative toxicity based on milligrams of the cation at the LD<sub>50</sub> dose of the salts of penicillin is (increasing toxicity): Na, Sr, NH<sub>4</sub>, Ca, K and Mg, while the relative toxicity based on milligrams of the cation at the LD<sub>50</sub> dose of the acetates is (increasing toxicity): Na, Sr, NH<sub>4</sub>, K, Ca and Mg.

The toxicity of salts of penicillin is evidently primarily due to the cations used in their preparation.

**Studies on penicillin. II. Observations on therapeutic activity and toxicity.** Goeffrey Rake, Clara M. McKee, Dorothy M. Hamre and Carol L. Houck. *J. Immunol.*, Baltimore, **48**: 271-289, May 1944.

Experiments have proved that the therapeutic efficacy of penicillin can be determined accurately in vitro. In comparison with other antibiotic products from the growth of unicellular organisms it has first and foremost the features of high activity, high solubility, and low acute toxicity. It is effective when administered locally or systemically.

In comparison with the sulfonamides, penicillin shows many advantages. It is definitely bactericidal and not merely bacteriostatic. The order of magnitude of activity against many of the gram-positive cocci is many times greater than that of the sulfonamides. Moreover, penicillin is not inhibited by substances such as pus and tissue fluids which counteract the action of sulfonamide drugs.

Penicillin, when given subcutaneously in mice, is present in the urine in high concentration within 30 minutes, and when 100 Oxford units are administered it is still to be found in appreciable amounts 8 hours later.

Penicillin has proved to be a substance of very low acute toxicity when given either orally or parenterally. In the purer forms given as a single dose, the toxicity is so

low that it may be considered as non-existent. Even the cruder preparations, in which only 5 percent or less is present as active penicillin, are many times less toxic for animals than any other well-known antibiotic substance.

**Blood agar plates.** Robb Spalding Spray. *J. Lab. & Clin. Med.*, St. Louis, **29**: 538, May 1944.

The necessity of keeping a constant supply of sterile blood for blood agar plates commonly used for cultures of streptococci, pneumonococci, gonococci and for hemophilic bacteria has been somewhat of a problem in the small clinical laboratories.

The Department of Medical Bacteriology and Public Hygiene of the West Virginia University School of Medicine has found the following procedure helpful: Blood specimens, which have been collected aseptically, are received daily for serologic examinations. On these, a clot is broken loose with a sterile loop, then the tubes are placed in the refrigerator. When the clot has retracted, only the minimum amount of serum required for the test is drawn off aseptically. The tube containing the clot and residual serum is held in the refrigerator at about 6° to 7° C. From the contents left in the tube it is possible to make one and sometimes two blood agar plates rich enough in color and in serum to serve excellently both for enrichment and for detection of alpha or beta hemolysis.

If the blood is collected and handled aseptically, there is rarely a contamination in such plates. Since they are poured immediately before streaking, an occasional isolated contaminating colony is of little importance. It is emphasized that these plates be freshly prepared as minute colonies develop on standing and can be distributed by the loop if inoculated on the following days.

It is suggested that the tubes be dated and the most recent ones used.

**An improved Pappenheim stain for gonococci.** Maxwell M. Barritt. *Brit. M. J.*, London, **No. 4344**: 494, April 8, 1944.

The author has modified his previous



ormula for a Pappenheim stain for gonococci. The formula which he now uses is as follows:

Methyl green (Gurr), chloroform-treated, 0.1-0.5 percent.....	100 cc.
Methyl alcohol, absolute.....	10 cc.
Pyronine G. (Conn. Grüber, B.D.H., or Gurr) .....	0.5 gm. or more
Phenol .....	1.0 gm.
Glycerol .....	20 cc.

This stain probably can be kept indefinitely since some the author prepared in April 1943 gives the same results as when it was fresh.

**A distinctive test for sulfadiazine.** Harry W. Raybin. J. Am. Pharm. A., (Scient. Ed.), Washington, 33: 158-159, May 1944.

The author has devised a simple test which will distinguish sulfadiazine from the other common sulfonamides. While the test may be performed on sulfadiazine, the 2-aminopyrimidine moiety is responsible for the reaction. Therefore, it is preferred to heat the sulfadiazine to obtain a sublimate of 2-aminopyrimidine.

For the purpose of this test 0.1 gm. sulfadiazine is heated in a small test tube over a low flame until it is melted and a ring of sublimate is formed. After cooling, some of the sublimate is scraped off and used directly in the test without further purification.

The procedure of this test is given as follows: A 5 percent alcoholic solution of resorcinol serves as the reagent. Dissolve a few milligrams of the 2-aminopyrimidine sublimate in 1 ml. of the reagent and add 1 ml. of concentrated sulfuric acid. The temperature rises to about 75° C. and a deep red color is produced. If the reaction product is diluted with 25 ml. ice water and neutralized with ammonia, the color changes to blue with a reddish tinge. If sufficient aminopyrimidine (0.1 gm.) has been used, and the reaction product poured on some cracked ice and neutralized with sodium bicarbonate, a purple solid may be isolated, which gives a deep blue with ammonia or alkali. The acid form is

reddish brown with a bronze reflex similar to fuchsin. The test is very delicate, and the red color may be obtained with 0.01 mg. of 2-aminopyrimidine.

The author states that the color possibly is due to the formation of malonic aldehyde formed by hydrolysis of the 2-aminopyrimidine and to a subsequent condensation of this aldehyde with resorcinol. An attempt now is being made to study the chemistry of the colored reaction product.

**Dihydroxypropyl bismuthate.** Larry M. Wheeler, R. A. Kuever, E. G. Gross and R. Nomland. J. Am. Pharm. A., (Scient. Ed.), Washington, 33: 156-158, May 1944.

A new method is reported for the preparation, isolation and purification of a series of new bismuth compounds. A series of such compounds has been prepared including dihydroxypropyl bismuthate, trihydroxybutyl bismuthate, the three isomeric pentahydroxyhexyl bismuthates, and pentahydroxycyclohexyl. Dihydroxypropyl bismuthate has been studied pharmacologically and clinically, and preliminary pharmacologic experiments have been made on trihydroxybutyl and pentahydroxyhexyl bismuthates. A description of this new method is given in detail.

Because the bismuth is present in these compounds as the bismuthate and not as a free ion, members of this series do not coagulate and precipitate protein, and they are stable within a pH range of from mild acidity to extreme alkalinity. This stability allows these compounds to pass through the stomach and remain soluble in the normally alkaline intestinal fluids and makes possible intestinal absorption in amounts previously impossible. Therefore, it now appears that wider margins of safety, as well as high and more uniform blood levels of bismuth, are possible during oral administration as compared to the standard intramuscular route previously employed. Compounds of this series are suitable for intramuscular injection, with both the advantages and disadvantages of the water-soluble group.

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## PUBLIC HEALTH ADMINISTRATION

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### **Venereal diseases in industry: Their control as a public health function.**

Richard A. Koch. *Indust. Med.*, Chicago, 13: 302-306, Apr. 1944.

Venereal disease case finding and case holding can be best managed by the health department as an unbiased official agency legally responsible for these activities. Industrial venereal disease control should include education of plant management as well as the industrial employee. The best approach to case finding is through education and serologic surveys. A serologic survey made in the San Francisco area on approximately 8,000 industrial workers disclosed a rate of 50 per 1,000 among unskilled laborers, 46 in semiskilled laborers, 37 in skilled laborers, 43 in office workers, 11 in professional workers, or an average of 43 per 1,000 for all classes. The highest incidence rate was found among Negroes (20 percent) and the lowest among white workers (3.2 percent), with an incidence of 13 percent among Filipinos and 10 percent among Mexican workers. Seventy percent of these workers were previously not known to be syphilitic.

The routine survey diagnostic case-finding procedure for syphilis does not apply to the case finding of gonorrhea, chancroid and lymphogranuloma venereum in industrial workers. Owing to the characteristics of these diseases, they are not amenable to reliable survey laboratory diagnostic procedures. Therefore, the approach to the control of these diseases depends upon the educational aspects of the industrial venereal disease control program which should instruct the employee on the importance of a suspicious attitude toward all genital lesions and encourage him to seek medical advice upon the appearance of any genital symptoms.

In an evaluation of the cost of syphilis to man it is estimated that an average of 1½ days per man are lost each year as a result of venereal disease. In addition, the

disease decreases the life expectancy by approximately one-fourth.

The author points out that it is the function of the public health department to find syphilis in industry and the responsibility of the physician to treat it adequately.

### **Treatment of venereally infected men in the Armed Forces.** Editorial. *Northwest Med.*, Seattle, 43: 130, May 1944.

The writer says that apparently some civilian physicians are not aware of the fact that men in the Armed Forces who become infected with venereal diseases, should be treated exclusively by commissioned Army and Navy officers. A letter from the District Medical Officer of the Thirteenth Naval District clarifies any misunderstanding regarding treatment of these cases in the Navy, and his remarks are equally applicable to infected men in Army service.

The Medical Officer says that every effort should be made by Navy medical officers to locate and treat all venereally infected individuals under their jurisdiction. While the number of infections concealed in this manner may be small, all personnel should be made cognizant that this form of concealment is subject to punishment. Information indicates that most of the men seeking civilian treatment are in the higher rated groups of enlisted men. Civilian physicians should be indoctrinated, as a patriotic service, not to treat naval personnel for venereal diseases without informing Navy medical authorities. The surreptitious administration of sulfa drugs to Navy personnel, particularly the aviation branch, may lead to fatal accidents.

### **Blood donor policies.** Roscoe D. Leas and John J. Grady. *Bull. Acad. Med. Cleveland*, 29: 11, 17, May 1944.

In response to inquiries, the American Red Cross Blood Donor Service gives an outline of the procedure followed in regard to those donors who have positive serologic tests. The Kline test is made on each pint of blood collected. If found positive the name of the donor is reported to the physician in charge of the Blood Donor



service. The files and all correspondence are confidential. A letter, or if necessary a series of letters, is then sent to the donor and to the donor's physician. In case there is no response to these efforts, the board of health of the community in which the donor resides is then notified.

**Venereal diseases.** J. R. Heller, Jr., Chairman. Clinics, Philadelphia, 2: 1106-1125, Feb. 1944.

This is a symposium on war medicine, made up of teaching panels presented at the 51st Annual Meeting of the Association of Military Surgeons of the United States, held in Philadelphia on Oct. 22-23, 1943.

The topics under discussion covered the treatment of syphilis, including the rapid-cure method; the prophylaxis and treatment of gonorrhea; syphilis in a pregnant woman; the diagnosis and treatment of chancroid and lymphogranuloma, false positive Wassermann reactions; the possibility of a soldier with neurosyphilis being returned to active service; public health education; the sulfonamide resistant cases of gonorrhea, and the use of the sulfonamides as a prophylaxis for gonorrhea. These subjects were discussed in relation to members of the armed services.

In regard to the use of sulfonamide compounds as a prophylaxis for gonorrhea: The Navy does not authorize their use generally while the Army does approve this form of prophylaxis in units in which the gonorrhea rate is high, that is, over 50 per 1,000 per year.

The authorities participating in the subjects under discussion included Cox, Moore, Heller, Schwartz, Turner and Keefe.

**The administrative control of syphilis.**

Russell E. Teague. Kentucky M. J., Bowling Green, 42: 102-108, Apr. 1944.

In 1938 the Kentucky State Department of Health, upon receipt of Federal funds and with advice and assistance of the Committee on Venereal Disease Control of the State Medical Association, undertook an intensive syphilis control program. It was estimated that at this time from 2 to 3 percent of the white population and 17 to 25 percent of the Negroes gave evidence of syphilitic infection. A survey in 1940 showed that 62 to 70 percent of early cases were lapsing before receiving minimum adequate treatment; however, the incidence of new infections was decreasing slightly. The prenatal and premarital laws had become effective.

After mobilization, the epidemiologic program was intensified. Clinics were expanded; case-finding and case-holding investigators were employed. Methods of reporting and tracing sexual contacts of patients in civic life and in military personnel were developed. Known houses of commercialized prostitution were closed under a new law. Infected promiscuous girls were generally quarantined and isolated, and intensive therapy was used in a limited number of infectious cases.

From 1936 to 1943, the number of doses of free drugs distributed increased 883 percent; the number of treatments administered in public health clinics increased 120 percent; the number of serologic tests, 1,641 percent; the number of syphilis patients under treatment in clinics, 214 percent; the number of new cases of syphilis reported to the State Department of Health, 120 percent.

It is difficult to evaluate the results of the past efforts. The effectiveness of the present program can be seen best in the declining rates in military personnel stationed in the State; while this is somewhat less than for the military personnel in the nation as a whole, the rates have shown a marked downward trend.

**New Cases of Syphilis and Gonorrhea in States, Territories, and Possessions**  
 Health officers' monthly statements: Reported for the first 10 months of the fiscal years  
 1943-44 and 1942-43

Area	Cases of syphilis and gonorrhea reported for first 10 months of fiscal years below											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital			
1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	
United States†	388,889	471,414	65,565	71,269	104,464	125,319	172,054	210,403	11,359	13,894	251,354	228,863
Alabama-----	14,724	17,960	1,846	2,818	3,315	5,007	3,453	5,358	301	433	5,341	7,251
Arizona-----	2,332	2,251	565	315	644	516	895	1,231	113	103	1,451	893
Arkansas-----	8,418	14,618	1,048	1,511	2,833	5,694	3,270	5,882	184	256	3,805	4,058
California-----	27,737	26,758	4,642	3,717	6,403	6,032	15,387	15,213	804	782	29,085	20,043
Colorado-----	3,262	4,385	787	851	916	1,062	1,434	2,280	125	192	2,741	2,179
Connecticut-----	2,363	2,401	268	223	1,078	775	593	817	85	83	1,264	1,174
Delaware-----	841	916	138	110	236	222	217	229	22	25	180	135
Dist. Columbia-----	6,950	6,134	818	706	1,603	1,594	4,221	2,721	112	104	3,337	2,819
Florida-----	23,941	29,289	2,677	4,423	7,732	7,455	10,857	14,592	498	686	13,548	11,554
Georgia-----	12,935	23,648	2,598	3,300	5,164	11,181	4,778	8,553	390	613	8,135	10,126
Idaho-----	486	372	207	112	92	27	146	181	14	19	726	269
Illinois-----	23,372	24,237	3,092	2,766	5,198	4,950	14,602	15,888	480	633	19,210	16,418
Indiana-----	7,197	11,414	1,079	1,414	694	382	2,672	4,465	208	366	2,777	3,841
Iowa-----	2,037	2,414	395	302	528	770	901	1,085	131	92	1,478	1,502
Kansas-----	2,480	3,395	492	662	515	440	1,380	1,687	93	96	1,591	2,338
Kentucky-----	5,956	10,760	930	1,319	1,301	2,349	2,524	4,596	237	334	3,089	3,687
Louisiana-----	15,020	15,426	2,630	2,117	3,948	4,550	4,022	7,034	393	435	12,147	6,281
Maine-----	908	794	197	187	123	144	461	326	85	77	1,184	564
Maryland-----	11,858	14,631	1,390	1,021	1,633	1,185	2,637	1,741	110	174	5,650	6,506
Massachusetts-----	4,734	4,572	963	826	(§)	(§)	3,477	3,530	292	214	4,186	3,801
Michigan-----	14,330	11,360	2,083	1,605	3,816	2,471	6,102	5,098	353	400	9,339	7,289
Minnesota-----	2,069	2,560	201	198	240	265	1,492	1,945	96	93	1,610	1,240
Mississippi-----	21,758	33,226	7,379	8,202	6,139	11,229	7,302	12,530	943	1,265	24,752	27,547
Missouri-----	8,587	7,858	1,500	1,259	2,224	1,526	4,162	3,773	282	205	5,055	3,765
Montana-----	355	426	88	140	58	32	140	201	7	8	254	320
Nebraska-----	1,146	1,764	164	208	487	409	421	1,054	31	61	1,187	1,399
Nevada-----	650	674	48	0	100	104	441	430	18	11	314	218
New Hampshire-----	235	273	33	25	52	24	123	192	15	20	147	154
New Jersey-----	9,282	9,286	1,093	1,104	2,774	2,438	5,030	5,325	352	311	4,311	5,532
New Mexico-----	1,738	1,937	361	331	408	432	887	1,059	72	97	1,170	678
New York-----	29,920	31,176	4,475	3,273	5,306	4,872	18,890	22,144	850	1,045	16,019	13,508
North Carolina-----	9,314	14,794	2,518	3,099	3,754	6,236	2,873	5,107	169	352	7,495	9,280
North Dakota-----	252	272	80	33	43	46	71	126	20	15	223	211
Ohio-----	19,527	19,750	3,113	2,847	4,730	4,574	10,120	11,462	783	867	4,797	3,720
Oklahoma-----	6,822	9,232	912	1,357	1,873	3,521	2,515	2,294	248	266	4,443	3,774
Oregon-----	1,713	1,203	522	230	127	109	1,010	781	54	66	2,157	1,112
Pennsylvania-----	11,031	5,866	1,454	1,016	4,061	3,296	4,025	896	524	132	(*)	(*)
Rhode Island-----	876	945	98	36	90	72	606	725	20	33	700	444
South Carolina-----	12,939	17,003	2,694	3,556	5,089	7,148	4,554	5,657	296	362	5,060	4,950
South Dakota-----	402	440	72	83	73	144	200	163	29	19	301	235
Tennessee-----	15,769	19,978	2,008	2,553	6,397	6,770	6,773	9,949	364	480	11,497	9,039
Texas-----	20,718	40,093	2,734	5,082	6,339	8,491	8,467	13,223	653	1,445	9,328	13,552
Utah-----	705	549	177	181	97	64	416	290	15	10	528	635
Vermont-----	237	224	72	112	76	1	77	100	11	11	168	148
Virginia-----	12,667	15,115	3,454	4,424	4,765	5,471	4,058	4,687	232	315	10,204	7,226
Washington-----	3,515	2,902	698	574	761	415	1,577	1,545	107	100	6,377	4,579
West Virginia-----	3,058	4,640	527	721	486	800	709	1,278	104	154	1,972	1,918
Wisconsin-----	758	934	142	179	0	1	608	735	8	20	860	666
Wyoming-----	975	559	103	141	152	23	478	225	26	14	161	283
Territories and possessions												
Alaska-----	81	136	49	42	15	34	14	33	1	6	387	461
Hawaii-----	832	940	165	244	98	111	545	473	59	52	1,480	1,177
Puerto Rico-----	12,322	7,868	1,321	1,688	2,225	1,206	4,205	2,751	1,668	1,384	3,224	2,568
Virgin Islands-----	164	194	27	48	98	109	32	26	6	8	240	135
Actual total of U. S., Territories and possessions†	402,288	480,552	67,127	73,291	106,900	126,779	176,850	213,686	13,093	15,344	256,685	233,204

\* Data not available.

\*\* Includes "not stated."

† Based on States reporting in both fiscal periods.

§ Includes all reported cases.

† Included in late and late latent.

‡ Based on 48 States.



**New Cases of Syphilis and Gonorrhea in Cities of 200,000 Population and Over**  
 Health officers' monthly statements: Reported for the first 10 months of the fiscal years  
 1943-44 and 1942-43

Cases of syphilis and gonorrhea reported for first 10 months of fiscal years below

City	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital			
	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43
Total†-----	138,934	141,240	116,169	114,879	329,163	325,941	358,500	365,069	32,606	32,863	66,339	58,140
Akron-----	730	1,083	104	149	170	212	400	674	42	48	266	223
Atlanta-----	2,271	3,410	589	780	694	1,203	1,076	1,396	23	31	1,162	830
Baltimore-----	9,139	11,175	1,066	743	1,069	779	2,152	1,264	63	59	2,204	2,926
Birmingham-----	4,015	5,478	253	480	1,031	1,600	1,003	1,410	69	133	454	766
Boston-----	1,526	1,721	296	264	0	147	959	1,104	41	61	1,111	990
Buffalo-----	1,643	1,554	198	132	186	27	1,218	1,341	41	54	779	849
Chicago-----	13,747	13,810	2,092	1,929	3,132	2,830	8,238	8,687	285	364	11,065	10,740
Cincinnati-----	2,528	3,076	350	345	(*)	(*)	2,178	(*)	(*)	(*)	793	835
Cleveland-----	3,609	3,330	671	559	1,133	783	1,723	1,875	82	113	1,282	1,183
Columbus-----	1,322	1,340	285	172	291	275	688	842	38	51	279	322
Dallas-----	2,174	2,746	415	358	468	480	1,272	1,875	18	31	628	954
Dayton-----	1,448	1,067	159	155	403	199	837	673	49	36	573	223
Denver-----	1,566	1,908	360	361	419	364	582	1,092	45	48	1,450	1,003
Detroit-----	10,026	7,228	1,290	974	3,143	1,773	5,411	4,326	182	155	4,888	4,155
Honolulu-----	452	570	50	203	60	74	297	258	44	35	925	937
Houston-----	1,696	3,697	299	260	595	1,245	751	2,094	51	98	1,861	1,000
Indianapolis-----	1,943	3,443	474	527	81	70	467	802	24	30	1,02	408
Jersey City-----	399	588	42	47	80	95	267	420	20	26	35	44
Kansas City-----	1,513	1,717	258	242	286	223	901	1,085	59	73	843	816
Los Angeles-----	9,498	8,514	0	362	3,776	2,681	5,434	5,229	288	242	4,289	4,123
Louisville-----	1,739	2,062	302	248	319	368	749	1,242	28	49	788	1,039
Memphis-----	5,941	6,624	499	567	2,764	2,391	2,569	3,459	86	89	4,334	2,481
Milwaukee-----	413	476	45	68	5	5	347	397	3	6	168	97
Minneapolis-----	637	716	103	75	117	115	395	512	19	18	678	554
Newark-----	1,820	2,053	244	287	484	560	1,039	1,166	53	40	724	829
New Orleans-----	2,103	2,556	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	1,831	1,037
New York-----	20,806	21,962	3,794	2,979	4,669	4,162	11,548	13,576	525	574	11,537	9,418
Oakland-----	1,478	1,162	154	134	374	297	892	683	38	28	1,224	786
Okla. City-----	1,774	1,872	188	285	449	609	536	610	40	24	891	676
Omaha-----	486	915	45	101	234	172	175	592	23	39	411	575
Philadelphia-----	8,185	3,213	(*)	251	(*)	(*)	(*)	(*)	(*)	(*)	782	(*)
Pittsburgh-----	8,513	7,124	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	119	235
Portland-----	755	621	217	121	46	41	479	427	13	33	941	530
Providence-----	415	438	58	25	40	29	271	350	8	11	140	123
Rochester-----	(*)	266	(*)	35	(*)	2	(*)	218	(*)	11	(*)	187
St. Louis-----	5,222	3,639	698	455	1,709	1,088	2,642	1,959	163	112	1,773	908
St. Paul-----	245	437	28	48	36	56	160	306	11	15	237	162
San Antonio-----	1,028	1,550	141	113	262	466	585	961	31	54	1,069	820
San Diego-----	940	875	107	88	271	303	492	469	32	14	839	563
San Fran.-----	2,459	2,920	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	1,812	2,489
Seattle-----	1,148	1,144	157	143	207	162	712	754	18	20	1,445	1,188
Syracuse-----	810	789	23	18	23	2	742	752	22	17	284	163
Toledo-----	772	637	115	82	137	115	491	407	29	32	105	140
Wash., D. C.-----	6,950	(*)	818	(*)	1,603	(*)	4,221	(*)	112	(*)	3,337	(*)
Actual total†	145,884	141,506	16,987	15,165	30,766	25,943	64,899	65,287	2,718	2,874	70,458	58,327

\* Data not available.

\*\* Includes "not stated."

† Based on cities reporting in both fiscal periods.

‡ Includes all reported cases.

<sup>1</sup> Based on 42 cities.

<sup>2</sup> Based on 36 cities.

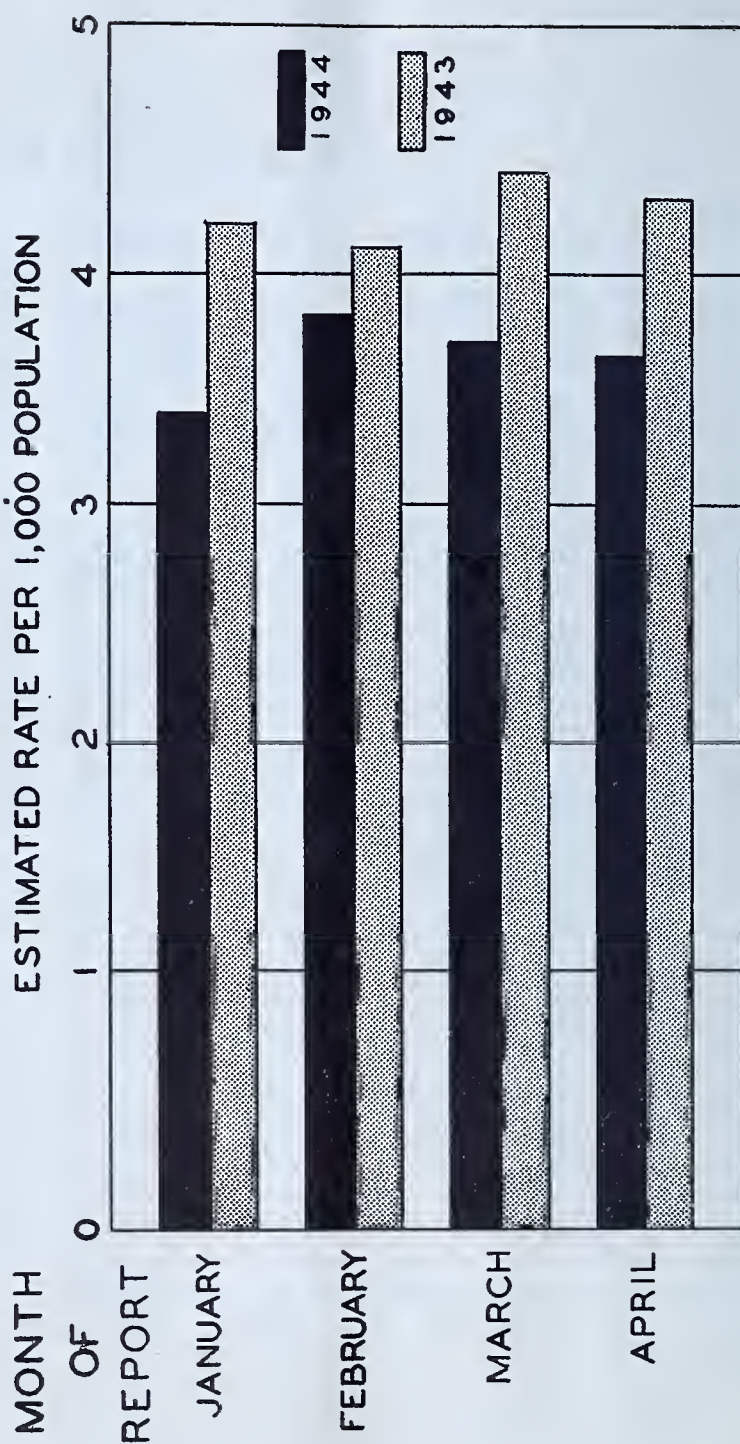
<sup>3</sup> Based on 35 cities.

<sup>4</sup> Based on 39 cities.

# ANNUAL SYPHILIS CASE RATES IN THE UNITED STATES BASED ON PROVISIONAL MONTHLY DATA

1944 AND 1943

ESTIMATED RATE PER 1,000 POPULATION





# Venereal Disease

## Information

VOLUME 25  
NUMBER 9

SEPTEMBER 1944

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FEDERAL SECURITY AGENCY  
UNITED STATES PUBLIC HEALTH SERVICE

THOMAS PARRAN, *Surgeon General*

Editor: J. R. HELLER, Jr., *Medical Director*  
*Chief, Venereal Disease Division*

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# The Rapid Treatment Center Program of Texas

Melford S. Dickerson, M. D., Director, Division of Venereal Disease Control,  
Texas State Department of Health

The rapid treatment center program is a part of the general venereal disease control program of Texas. The State Department of Health determines the need and location of the centers and then makes application to the Federal Works Agency for funds for maintenance and operation by submitting a budget and a justification on the basis of its need. The United States Public Health Service and the State health department likewise contribute funds and professional personnel.

Problems encountered in setting up the program included adverse public opinion toward this type of establishment; difficulty in locating a satisfactory facility that could be converted by renovation, particularly in communities possessing the principal reservoirs of infection; scarcity of adequately trained personnel; shortage of essential critical materials, and lack of understanding between the operating and cooperating agencies in the venereal disease control program.

In spite of these obstacles the first center was opened in El Paso in March 1943. A center in Mineral Wells was opened in April 1943, one in Corpus Christi in August 1943, one in San Antonio in September 1943; one in Waco has been opened recently. This makes a total of 5 centers now in operation in Texas. Two more have been approved, one for the Houston-Beaumont-Galveston area and one for the Fort Worth-Dallas area, the former to be established in the Galveston State Psychopathic Hospital within the next 60 to 90 days, and the latter to be located in a new facility close to Dallas.

In view of the size of Texas and the location of the largest cities, the centers were established to serve definite areas. At present the State is divided into 8 areas. When all centers are in operation, each of

7 of these areas will be provided with one. Recently an agreement was made by the State health officers of Texas and New Mexico whereby patients from the southern part of New Mexico will be received by the El Paso center, and patients from the Texas Panhandle, which is the eighth area and the only one without a center, will be admitted at Albuquerque. Insofar as possible each center contains sufficient beds for the community need, although some centers have not been able to meet the demand. It is hoped to increase the bed capacity, which now varies from 50 at Mineral Wells to around 400 at Galveston, with a total of 950 beds for all centers. The centers are becoming more popular, and voluntary admissions are increasing in number.

To date a total of 2,061 patients have been treated in the centers at an average cost per patient of \$68.46. The average food cost per patient per day is 55 cents; the average total cost per patient per day is \$3.20. The total cost of operating the first 4 centers to date is approximately \$160,000.

In January 1944, an Advisory Committee for the Texas Rapid Treatment Centers was organized and it consisted of a representative each of the U. S. Public Health Service, the U. S. Federal Works Agency, the Social Protection Division of the U. S. Federal Security Agency, and the Texas State Department of Health. The initial task of this committee was to determine the exact functions of each one of the cooperating agencies represented in this program. With this in mind each agency was aware of the others' limitations. Basic policies were adopted, relationships and responsibilities established, a personnel roster drawn up, and finally, operating procedures formulated. All of this material was compiled into a manual of operation, which is used as a guide in each center. Memoranda on administrative procedure

Delivered at the Mexico-United States Border Health Conference, May 30 to June 1, 1944, El Paso, Texas.

are sent to the centers from the central office and explain such matters as the setting up of a canteen fund, use of a revolving fund, patient labor, budget revisions, educational projects, sanitation, recreational equipment, and many others.

The State Department of Health maintains and operates the centers with the listed Federal agencies as consultants.

The principal functions of the Advisory Committee are (1) formation of broad general policies, (2) maintenance of a common understanding between operating and co-operating agencies, (3) determination of needs of the centers by making periodic joint tours of the facilities, (4) recommendations of budgetary readjustments.

The State Health Officer is administratively responsible for the operation, control and maintenance of the centers. The Director of the Division of Venereal Disease Control is in charge of the actual operation; he is assisted by a State business manager and a field consultant for the centers. Within the center the medical officer is in charge of all its activities and is responsible to the Director of the Division of Venereal Disease Control. He is assisted by the nurses, a social worker and a liaison officer, and by the local business manager. The latter is responsible for the work of matrons, cooks, maintenance man, transportation officer, guard, stenographers, and clerks. The function of the liaison officer is to improve case-finding procedures in the entire area served by the center; he receives technical assistance from the epidemiologist, Division of Venereal Disease Control. All the centers are serviced by State branch laboratories which are located either within the centers or nearby. The record analyst keeps accurate medical statistical data on all patients admitted. The director of the vocational and recreational program organizes the patients' time into a balanced program of work, rest and education. The placement officer assists patients in securing suitable employment upon their discharge from the center. He works in close cooperation with the social worker and the vocational and recreational program director. The personnel of the centers

are paid out of three separate budgets. The medical officer-in-charge, the supervisory nurse and the record analyst are employed by the U. S. Public Health Service; they are assigned to the State Health Officer who assigns them to the different centers. Staff nurses and social workers are paid by the State; all other personnel, with Latham Act funds.

All physicians in the centers have had postgraduate training in the intensive methods of venereal disease therapy under the direction of Dr. Udo Wile, Ann Arbor, Mich. In the treatment of syphilis various methods are employed, including the 8-day intravenous drip treatment and the Eagle-Hogan method which involves an 8- to 10-week stay in the center. For gonorrhea, the sulfonamides have been used extensively, but recently penicillin has displaced them to a large extent. One center obtained cures in all of a series of 120 cases of gonorrhea treated with penicillin. A total of 150,000 Oxford units given in 15 to 18 hours is the accepted dosage at the present time. The other venereal diseases are treated by established methods.

Since the primary aim of the rapid treatment center is to render patients with venereal disease noninfectious as quickly as possible by the most intensive methods, patients must be carefully selected. The following types of cases are accepted for treatment: (1) Syphilis—primary, secondary, relapsing, early latent, and early congenital; (2) gonorrhea—all types are admitted but preferably those cases that have been resistant to sulfonamides; (3) chancroid, lymphogranuloma venereum, and granuloma inguinale constitute a very small percentage of admissions.

Persons not acceptable for treatment include those who are feeble-minded; those who have psychoses due to syphilis; psychoses associated with venereal disease; chronic disease such as tuberculosis or cancer; acute infections such as pneumonia or meningitis; other communicable disease associated with venereal disease; invalidism, and those charged with offenses against the law.

A very definite policy for admission of



patients to these centers has been established. Requisites for admission are as follows: (1) The venereal diseases must be in the infectious stage; (2) all infections must have been diagnosed on the basis of laboratory reports; (3) a preadmission social and medical history must accompany the patient; (4) a signed, health officer's quarantined commitment may or may not be necessary.

Patients are sent to the centers from private physicians, venereal disease clinics and private hospitals. They may make voluntary application for diagnosis, and treatment if necessary. In cases of arrested promiscuous women and prostitutes in whom a positive diagnosis is made by the health officer and of patients found as a result of contact investigation, treatment is compulsory. Every effort is being made to popularize these facilities through education, and it is hoped that soon most admissions will be voluntary.

The transportation of patients to and

from the centers is handled in many ways. Each center has a station wagon which transports to it patients from health units and departments within the entire area served by the center. Patients also come to the centers either voluntarily or with supervisory escort on the common carriers such as bus, train, airplane or car. Traveling expenses are paid by the patient or by a social service agency.

In conclusion it may be stated that the Texas rapid treatment centers have an extremely useful function in venereal disease control. It cannot be said, however, that they are a complete solution to the venereal disease problem. Although more than 2,000 patients have received treatment in these centers, we still have to determine their effectiveness in reducing the prevalence of venereal disease. Their success depends principally upon a comprehensive and thorough system of case finding as a part of the local general venereal disease control program.

## A Sociologic Analysis of 304 Female Patients Admitted to the Midwestern Medical Center, St. Louis, Mo.

H. L. Rachlin, Surgeon (R)  
United States Public Health Service

The Venereal Disease Division of the United States Public Health Service, as part of the war program to reduce the incidence of venereal disease, has set up a number of rapid treatment centers throughout the United States, for the treatment of venereally infected women. It was soon recognized that a program restricted entirely to treatment of patients, without bringing to the attention of appropriate agencies the need for some form of rehabilitation for certain patients, would be ineffectual. A plan should be put into effect whereby the more stable of this group of women could be directed into war industry where the services of every able-bodied woman are essential in the war effort, and whereby the maladjusted and the emotionally disturbed woman could be

referred to appropriate social agencies in the community for further help and guidance. For this purpose the writer was directed to set up a sociopsychiatric program as a demonstration project at the Midwestern Medical Center in St. Louis, Mo.

After a brief period of observation, the writer became aware that the patients admitted to the center for treatment presented many behavior difficulties in addition to the disease for which they came for treatment. In order to know more specifically the type of patients with which the center was dealing, so that appropriate recommendations could be made for their redirection when discharged to the community, the writer made a study of 304 consecutive unselected patients admitted to

the center over approximately three months. Because of the rapid turnover at the treatment center and the short period of hospitalization, brief interviews, which would be sufficiently informative, were resorted to.

The following analysis is based on information gathered from these interviews with the 304 patients. The material was examined from the point of view of race, civil status, age distribution, age at marriage, residence, education, mental ability, employment and earning power, sexual activity and family background.

#### RACE AND CIVIL STATUS

Table 1 shows that the group was predominantly white,—211 white, 93 Negro,

TABLE 1.—*Race distribution*

	Married	Single	Total
White	142	69	211
Negro	56	37	93
Total	198	106	304

and the greater number were married, 198 married, 106 single.

#### AGE DISTRIBUTION

The age of the group ranged from 14 to 44 years, with the greatest number, 252, between 15 and 24. The unmarried group ranged from 14 to 20, the adolescent period.

TABLE 2.—*School grade distribution for St. Louis and other cities*

Grade	St. Louis		Transients		Other cities		
	White	Negro	White	Negro	White	Negro	Total
No schooling	0	1	0	0	0	0	1
1	0	0	0	0	0	0	0
2	0	2	0	0	0	0	2
3	1	1	1	0	3	0	6
4	2	0	1	0	0	1	4
5	3	4	1	2	3	1	14
6	4	4	2	0	6	1	17
7	18	6	3	1	11	1	40
8	28	20	10	5	19	2	84
High School							
1	6	10	4	0	10	1	31
2	17	8	11	0	9	1	46
3	4	9	2	1	3	1	20
4	5	6	5	1	11	..	28
College							
1	1	..	..	..	..	..	1
2	..	..	..	1	..	..	1
3	..	..	..	..	..	..	..
4	..	..	..	..	1	..	1
Unknown							
	..	3	4	..	1	..	8
Total	89	74	44	11	77	9	304



#### AGE AT MARRIAGE

The age at marriage ranged from 12 to 29 years, the largest number marrying between the ages of 15 and 19. It should be noted that there was very little difference in age of marriage between the Negro and white. Many married at a very early age, some as young as 12 and 13. The majority, 127, were married by their eighteenth year, the average age at which girls from better homes are still in school. This is not an accident; when questioned, the girls stated they married to escape an intolerable home situation with the belief that married life would be easier. Some married to legalize their desire for sexual activities. The girls from the less populated areas married at an early age because it was part of the mores of the locale. Some married soldiers in order to secure the Government allowance.

#### RESIDENCE

Of the 304 cases, 163 (more than half) were residents of St. Louis; 87 were from 38 smaller cities of Missouri (sent to the center by their local health officers); 54 were transients picked up in St. Louis. The majority of these 54 were residents of Missouri who came to St. Louis to work; they were considered transients because they were in St. Louis less than a year. Very few came from other States.

#### EDUCATION AND MENTAL ABILITY

Table 2 is a detailed analysis of the educational achievement of the group. There is essentially no difference in the scholastic accomplishment of the white and Negro, or of the St. Louisians and those of other cities. The range in achievement is from no education in one case to college education in three. Eighty-four had less than eighth grade, with 40 completing seventh grade. Eighty-four completed eighth grade, which is the largest number for any school year. One hundred twenty-five had some high school education.

The scholastic record suggests that we are dealing with a group who seem to have a more than average intellectual level. In order to more clearly evaluate this, two sets of tests, the Stanford-Binet (Terman-

Merrill Rev. Form M) and the Otis Beta B, were given to two separate groups. The Stanford-Binet, which is an individual test, was given to a group of 93. The Otis Beta B, a group test, was given to a group of 200. The results showed a discrepancy between the educational achievement and the actual mental ability. On the Stanford-Binet, Form M., the patients achieved a median mental age of 11 years 3 months, and a median I. Q. of 75.3. On the Otis, the results were somewhat higher, as they usually are in a group test. In the latter, they achieved a median I. Q. 80.3. Chart I is a graphic description of the results of the Binet test, and chart II is a graphic description of the results of the Otis test. Curve A in both charts represents the normal, or average distribution of the mental level of a given group. Curve B is the distribution of our group. Both B curves show a distinct swing to the left of the median. This is significant and reveals that we are dealing, in the main, with the intellectually inferior individuals of the community.

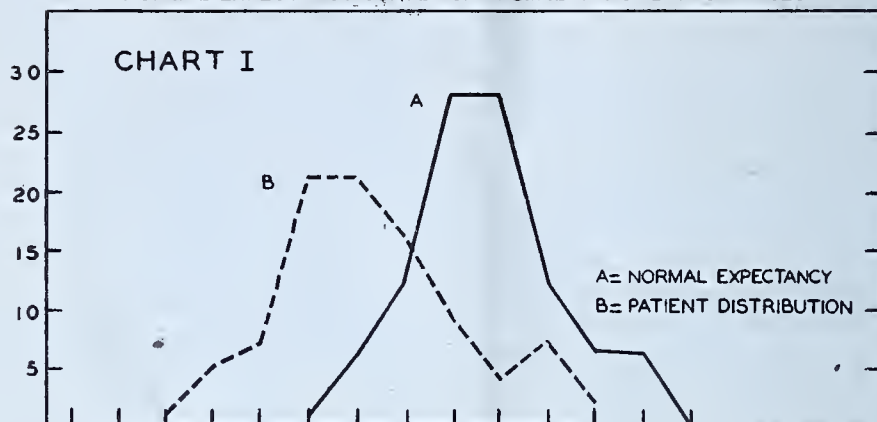
#### EMPLOYMENT AND EARNING POWER

In analyzing the employment of the group (table 3), it is significant that of the 304 patients, 232 were gainfully employed, and of the remaining 72, 24 were housewives, 5 were school girls. Only 21 were unemployed, and in 15 employment records were not secured. Of the whole group, only 3 were earning their living as prostitutes and 4 were supported by their paramours (they referred to themselves as "kept women").

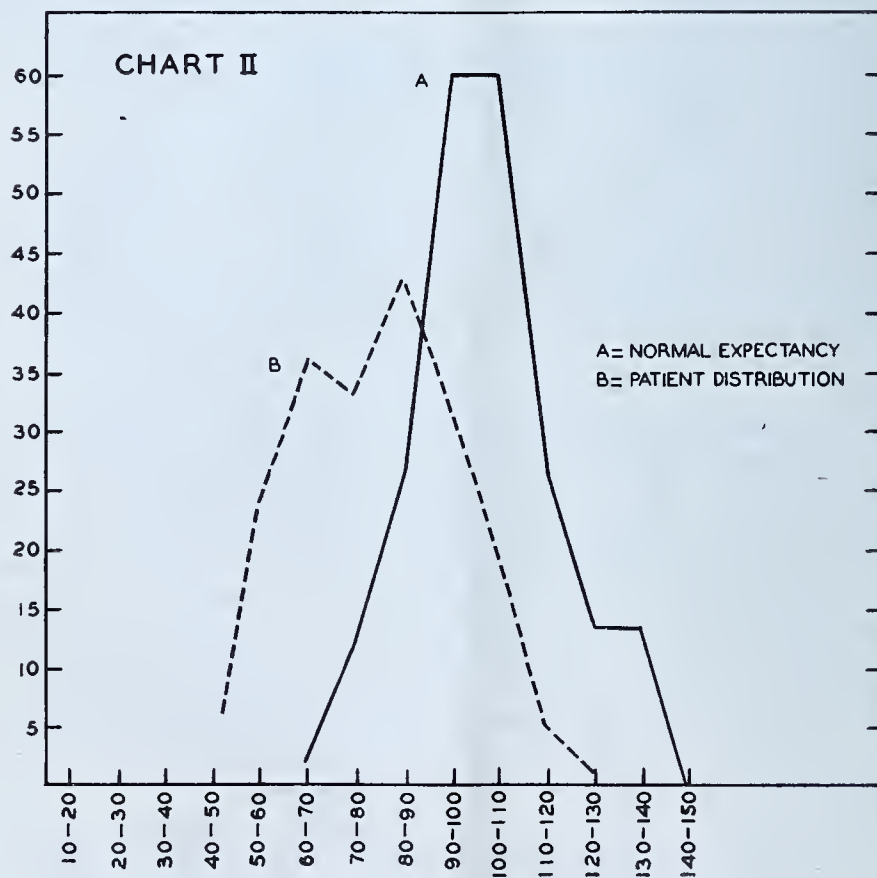
In classifying the type of employment, 37 different occupations were noted, and of these, 5 categories—the tavern girl, the dice girl, the night club entertainer, the burlesque entertainer, and the taxi dancer—definitely expose the girl to an unhealthy social environment. Only 15 girls were thus employed.

The average earning capacity of the individual was difficult to determine, as none had worked steadily over any given time. However, a rough estimate shows that the majority of the white women were earning from \$14 to \$24 a week; 22 earned

COMPARATIVE DISTRIBUTION OF THE I.Q.'S OF 93 UNSELECTED PATIENTS ON THE STANFORD-BINET SCALE (TERMAN-MERRILL REV. FORM M) WITH THE NORMAL EXPECTANCY CURVE FOR A SIMILAR NUMBER OF CASES



THE DISTRIBUTION OF I.Q.'S OF 200 FEMALE PATIENTS ON OTIS TEST OF MENTAL ABILITY BETA B





\$3 to \$12; 37 earned from \$26 to \$40, and 2 claimed they were earning \$75 a week. However, the writer questions the validity of their statements. The salaries of \$24 and up were earned by those employed in defense plants.

The earning capacity of the Negro group was much lower than that of the white group. The majority of the Negro women earned from \$8 to \$18 a week; 10 earned from \$20 to \$24; one earned \$32; two \$35; one \$40, and one \$50 a week. The majority of the Negro women were employed at less skilled occupations where the salaries are lower. Because of their emotional immaturity and lack of judgment, they have no appreciation of the value of money and, therefore, squander their earnings without any consideration for the future. Whether they earned \$15 or \$50 a week, the women spent the entire amount.

SEXUAL ACTIVITY

Table 4 shows the age of the first sex experience of the group. The majority of unmarried white girls had their first experience between 14 and 19, and the unmarried Negroes between 14 and 17. One white girl had her first sex experience as early as 11 years of age and another at 12, while one Negro girl had hers at 10 and another at 12. There were 15 unmarried mothers (11 white, 4 Negro).

Of the 198 married women in this group, 86 had their first sex experience prior to marriage. A very small number stated that this experience was with the man they married. Seventeen children were born out of wedlock to this group. There seems to be very little difference between the age at first sex experience of either the married and unmarried group or of the white and Negro.

As stated, of the 304 cases, 198 were married. We questioned why such a large number of married women should have venereal disease. Upon analyzing the marital status of this group we find that 86

\*For the purpose of this paper, under "living together" were considered even those whose husbands were in the Armed Forces but not previously separated.

TABLE 3

Types of employment	White	Negro	Total
Waitress	41	10	51
Defense work	37	4	41
Factory work	24	5	29
Housework	14	13	27
Laundry work	5	7	12
Tavern	8	1	9
Dishwasher	3	5	8
Prostitute and kept woman	5	2	7
Chambermaid	1	4	5
Clerk { office	4	1	5
{ store			
Cook	1	4	5
Salesgirl	4	1	5
Fountain girl	3	1	4
Cleaning store	2	1	3
Night club entertainer	1	2	3
Bus girl	0	2	2
Farmer	2	0	2
Truck driver	2	0	2
Beauty operator	0	1	1
Bookkeeper	1	0	1
Burlesque entertainer	1	0	1
Counter girl	1	0	1
Dice girl	1	0	1
Egg packer	1	0	1
Electrical worker	1	0	1
Elevator operator	1	0	1
Gasoline service station	1	0	1
Model	1	0	1
Practical nurse	1	0	1
Presser	0	1	1
R. R. reservation	1	0	1
Scrub woman	0	1	1
Seamstress	0	1	1
Taxi dancer	1	0	1
Telephone operator	1	0	1
Undergraduate nurse	1	0	1
Usher	1	0	1
Housewife	15	9	24
School girl	2	3	5
Unemployed	13	8	21
Unknown	7	8	15

were living with their husbands\*, 68 were separated, 40 divorced and 4 widowed.

Of the 86 living together, 21 admitted that they were unhappy in their marital state; 46, which included some of the 21, attributed their disease to their husbands. Several, whose husbands were in the Armed Forces, frankly admitted that they

TABLE 4.—*Age at first sex experience*

Single Women			Married women, prior to marriage	
Age	White	Negro	White	Negro
10	..	1	..	..
11	1	..	..	1
12	1	2	1	2
13	2	1	2	8
14	6	8	2	7
15	16	9	12	6
16	15	6	4	9
17	11	3	14	6
18	6	2	4	..
19	3	1	6	1
20	2	2	1	..
21	1	..	..	..
22	1	..	..	..
23	1	..	..	..
24	..	..	..	..
25	2	..	..	..

were lonely and felt the need to gratify their biologic urge. Others explained their infidelity as a spite reaction to their husbands' extramarital affairs. One was a mental defective with psychosis, who was not responsible for her behavior.

Of the 68 separated and 40 divorced women, many were married less than a year and some only a few weeks. The reasons for separation in most cases were very trivial. Such a high rate of separations and divorces, as compared with the normal population, is not surprising in view of the early age at marriage, the emotional immaturity, and the high proportion of intellectual inadequacy.

A small number of the girls claimed they were selective in their choice of male companions. A considerable number, on the other hand, admitted that they accepted the attention of men indiscriminately. Though they were promiscuous they resented any inference that they were prostitutes. This indiscriminate choice is a reflection of the ethical standards of the group. This behavior stems from either a lack of moral consciousness—that is, amoral behavior—or is the aggressive response of the individual, as expressed through sexual delinquency, toward the community.

## SOCIAL BACKGROUND

Conduct or behavior is not a phenomenon which arises spontaneously but is the result of the impact of environmental forces with which the individual comes in contact. Therefore, in order to understand the sexual transgression resulting in venereal disease, we must know the environmental factors which contribute to it.

From the patients' statements and the information secured through the Social Service Exchange, sufficient data were collected to make possible an analysis of the social background of 249 of the 300 cases. Of these 249, 129 (52 percent) came from broken homes, i. e., parents were separated, divorced, one or both parents were dead; a stepparent was in the home; the patient had been reared in foster homes, or had been born out of wedlock. Of the 120 patients whose parents were living together, no conflict was reported in only 42 cases. All of these 42 were in the married group; 21 attributed their infusions to their husbands and the remainder indicated marital difficulties.

In 69 cases, though the parents were living together, there was severe conflict between the parents because of alcoholism in one or both parents, incest in the home, personality difficulties, infidelity of father or mother, and mental disease of the parents. In 9 instances the patients revolted against severe and rigid discipline in the home. All of the unmarried group came from either broken homes or homes where conflict between parents existed.

Of the 149 cases which it was possible to clear through the Social Service Exchange, 102 were known to one or more agencies in the community because of need for financial assistance, medical care, personal problems or emotional difficulties requiring the services of such agencies as child guidance clinics, psychiatric clinic and Juvenile Court. This showed that we were dealing with an underprivileged group so insecure that they constantly required the props of society to help them in their health, in their support, and even in keeping their homes in order.



## CONCLUSION AND RECOMMENDATIONS

In reviewing the analysis, it is seen that we are dealing with a group of sexually promiscuous women who are of the adolescent and post-adolescent age. The majority have been married but are now either separated or divorced because they are unstable, emotionally immature, and intellectually handicapped, and cannot accept or understand the social responsibilities of married life.

The educational achievement is about eighth grade, but their intellectual acumen (median I. Q. 80) is markedly inferior to a normal sampling of the population. Almost all were employed in some gainful occupation and were earning subsistence incomes.

The sexual activities of the group began at an early age, because of the poor and inadequate environmental conditioning.

Of all the basic instincts, the sexual instinct is most rigidly controlled by our social mores; the socially conscious individual learns to control his sexual instinctive urge. Where the individual grows up in an environment of conflict and in-

security, the ordinary restraints may never be developed or they may break down in defiance of authority. Where the ordinary restraints have not been developed or where they have broken down, the individual indulges readily in the gratification of the sexual instinct without regard for consequences. Thus we see that venereal disease is not an isolated phenomenon, but is a link in a chain of events. Therefore, any plan for the treatment of venereal disease must take into consideration the social forces which have affected the individual who developed the disease which brought her to the treatment center.

Unless there is a social program of re-direction for certain of these individuals, they will return to their community upon discharge, revert to their former mode of behavior, become reinfected and then return to the center, thus setting up a vicious cycle.

It is for this reason that our treatment centers should recognize these problems and enlist the assistance of appropriate agencies. For the recognition of these problems skilled personnel is necessary.

## False Positive Serologic Tests for Syphilis in Several Members of a Family

Bernard Zuger, Surgeon (R), United States Public Health Service,<sup>1</sup> and  
Gordon B. Moffat, M. D., D.P.H.<sup>2</sup>

False positive serologic reactions for syphilis have within recent years become an important problem because of the widespread extension of routine testing to detect unsuspected syphilis. The associated epidemiologic evidence in any particular case has been among the more useful criteria for evaluating the significance of a positive reaction in the absence of clinical signs (1). A positive reaction obtained on the consort or on the immediate members of a family of a seropositive individual has been generally accepted as strengthening

the possibility that his own positive test is due to syphilis.

Only two instances have been reported in which false positive tests for syphilis have occurred simultaneously in more than one member of an epidemiologically related group. Lindau (2) reported a family in which the parents and their two children were all serologically positive for syphilis for one month following an attack of bronchitis. Smith (3) related the occurrence of positive reactions in two young siblings six weeks after mumps.

In the above cases, the false positive tests could be related to the onset of a definite illness. Although there have been a few reports [reviewed by Davis (4)] in the American literature and more in the

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foreign literature of false positive tests occurring in normal individuals or in those with recent mild upper respiratory infections, there are none to our knowledge in which more than one individual of an epidemiologic unit was involved. It is for this reason that the following report may be of interest.

EPIDEMIOLOGIC DATA

The W. family consisted of a mother 32 years of age, and three boys, R, J and D, 11, 10 and 8 years of age, respectively. The father was dead. This family came to the attention of the Kalamazoo City-County Health Department because a positive Kahn

by two other laboratories to which the serums were submitted. Physical examinations of the children on several occasions were completely negative.

In three weeks from the time the children were first seen, the standard Kahn tests became negative. Within two months, even the more sensitive presumptive Kahn tests were completely negative. It became obvious that we were dealing with false positive tests. Treatment had not been instituted.

The children had received no immunizations since infancy. During the year previous to the time they were seen at this clinic, they had lived together in two places.

"W." FAMILY

MEMBER	LABORATORY	NEG. KAHN INCLUDES PRESUMPTIVE "P" = PRESUMPTIVE "V" = VERIFICATION			
MOTHER R.W. 32 YRS.	KALAMAZOO	NEG. (ALSO NEG. IN 1934 AND 1938)			
1ST. CHILD R.W. 11 YRS.	DR. KAHN'S			3+ V-BIOLOGIC	NEG.
	LANSING			3+ TITRE 1:1	NEG.
	KALAMAZOO	4+	4+	3+ + P-3+	NEG.
2ND CHILD J.W. 10 YRS.	DR. KAHN'S			+ V-BIOLOGIC	NEG.
	LANSING			NEG. (±) NEG.	NEG.
	KALAMAZOO	4+	3+	+ P-3+	NEG.
3RD CHILD D.W. 8 YRS.	DR. KAHN'S			± V-BIOLOGIC	NEG.
	LANSING			NEG. NEG.	NEG.
	KALAMAZOO	4+	P-± NEG. + P-4+	NEG. P-2+ NEG. P-3+	NEG.

1943

SEPTEMBER

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EIGHT CHILDREN IN SAME CAMP WITH "W." CHILDREN  
AT SOME TIME BETWEEN AUG. 1 AND AUG. 28. 1943

C.E. 11 YRS.	KALAMAZOO	NEG.
C.W. 10 YRS.	"	NEG.
B.R. 10 YRS.	"	NEG.
D.U. 9 YRS.	"	NEG. P-4+
D.L.U. 7 YRS.	"	NEG. P-2+
C.D. 7 YRS.	"	NEG.
G.S. 6 YRS.	"	NEG. P-2+
M.M.	"	NEG.

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test had been found on R, the oldest, during a medical examination performed in anticipation of his being boarded in a foster home.

The mother and all three children were retested 7 days later. The results are indicated in the upper portion of the table. It will be noted that the mother's blood was negative, as it had been in 1934 and in 1938. All three of the children gave positive tests. Similar results were obtained

The first 11 months of this period they had lived on a farm with a family which consisted of the father and mother and five children varying from 5 years to 5½ months of age. The latter children had not been ill during the previous year. Kahn tests on the two oldest, with whom the W. children used to play, were negative.

For the month prior to their being referred to the clinic, the three W. children were at a local children's camp. During



most of their stay they had an upper respiratory infection which apparently was febrile and which did not interfere with their activities. The presence of the "cold" was subsequently confirmed by the director of the camp; from the description of the illness, it did not seem to differ clinically from any other mild upper respiratory infection. The lower portion of the table gives results of Kahn tests on the serums from seven children of the Juvenile Home in Kalamazoo and one other child, all of whom had been at the camp with the W. children. It may be noted that positive presumptive Kahn tests were obtained on three of the eight children and that these results were similar to those on the W. children at that time.

#### DISCUSSION

The simultaneous and rapid loss of specific flocculating strength of the three serums suggests a common antigenic cause which operated shortly before the children were seen. That this cause was the upper respiratory infection while in camp is suggested by the circumstantial evidence and by the fact that no other cause was apparent.

Similar considerations hold for the three contacts who gave presumptive Kahn positive tests. The Kahn presumptive test, while slightly less specific than the standard Kahn test, gives an incidence of positive tests on normal serums of less than 2 percent (5, 6). The Kalamazoo Health Department laboratory, in which the tests were done, had not had another positive presumptive Kahn test on a normal serum at the time these tests were done. The quality of its serologic work is of a very high order, as disclosed from the monthly checks on unknown serums which the Michigan State Department of Health laboratory has been conducting for several years.

The simultaneous occurrence of false positive tests in a family group or other contacts points to the need for caution in interpreting the significance of a serologic reaction from the epidemiologic evidence

alone. In the cases reported in this paper, the meaning of their positive tests became clearer as time elapsed and the serologic pattern unfolded. This period of waiting and observing has been stressed by Mohr, Moore and Eagle (1) and Davis (4) as likely to give the surest answer in the case of a suspiciously false positive serologic reaction. As has been noted by others, a positive serologic test alone is not an emergency.

The Kahn verification test was kindly done for us in Dr. Kahn's laboratory at the University of Michigan. In our cases the test was helpful, but the experience is obviously too limited to be generalized.

#### SUMMARY

An epidemiologic study of a family is reported on three of whose four members false positive serologic tests for syphilis were obtained simultaneously. These tests were traced as presumptively originating from a mild upper respiratory infection. Among a small number of contacts exposed to the same infection as the members of this family there was evidence that suggested that they were immunologically similarly affected.

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## DIAGNOSIS

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**Diagnosis of early syphilis.** Jerome M. Spatz. Correspondence. J. A. M. A., Chicago, 125: 739, July 8, 1944.

In an open letter to the editor Spatz says that clinical teaching has always stressed that a painless sclerotic solitary ulcer or "hard chancre" is the typical primary lesion of syphilis. In the 11 cases of early syphilis which in the past few years he and his associates have positively diagnosed by dark-field examination only 3 presented the classic type of primary lesion. The 8 others resembled ordinary chancroidal or balanitic ulcerations; they were not indurated, often were multiple and sometimes were painful. A recent case presented the typical picture of an ordinary nonspecific balanoposthitis complicating a phimosis with several tender ulcerated areas on the preputial mucosa, and the patient said he had had the condition several times in the past. It was quite a surprise when a spread was found to be teeming with *Treponema pallidum*.

The question is brought up as to how many latent or advanced cases of syphilis were not detected in their early stage simply because the primary lesions were so atypical or minor as not even to suggest the ruling out of syphilis by the examiner. Each and every clinical case presenting a genital ulcer of any description should be subjected to the darkfield laboratory examination.

**The effect of syphilis on the pregnant woman and her offspring. An analysis of one hundred cases.** Kate Freeman Miller. M. Rec., New York, 157: 345-349, June 1944.

A study of 100 syphilitic mothers delivered at the Queens General Hospital among 3,200 consecutive deliveries from November 1935 to May 1938 emphasizes the importance of routine serologic tests of mother's blood for syphilis.

The incidence of syphilis among the Negro women was 14 percent and among

the white women, 1.8 percent. The majority of the syphilitic mothers were ignorant of their disease.

The diagnosis of syphilis in the 100 cases was made by history in 14; discovery in a previous pregnancy through routine test in 22; manifest syphilitic offspring in 5; by routine test in present pregnancy in 44 multiparas and 15 primiparas.

Among the first 94 patients treated for miscarriage at the Queens General Hospital in November 1935, not one syphilitic mother was found. None of the miscarriages occurred later than 16 weeks' gestation.

Only 14 of the mothers received adequate treatment; one was delivered of a full term macerated fetus and 4 living children manifested positive Wassermann reaction at 6 weeks of age. Among the babies of 20 mothers who received inadequate or no treatment at all, only 6 were apparently normal. There were 3 macerated fetuses, 2 premature neonatal deaths, 9 infants with positive serologic tests at 6 weeks. In the offspring of 8 of the patients untreated in this pregnancy but treated previously, there was 1 macerated fetus, 3 infants with positive Wassermann reactions at 6 weeks, and 4 normal. Not one of the living syphilitic infants gave any of the clinical manifestations of syphilis during a 10-day puerperal period.

One fetal death may be ascribed to treatment. A mother received her second injection of an arsenical, only 0.1 gm. of neoarsphenamine being given. An arsenical hepatitis developed and she was delivered of a stillborn fetus. The mother recovered.

The most reliable criteria for the diagnosis of syphilis in the newborn are lesions of the skin and mucous membranes; positive serologic reactions after the fourth to the eighth week of life, and autopsy findings. All of the infants with negative cord blood reactions were found to have negative serologic reactions at 6 weeks. Treatment on the basis of a positive cord Wassermann reaction is of value only from the prognostic angle.

Blood taken from the babies on the seventh day closely approximated the reaction



of cord blood. In the first few weeks of life, the infant's blood may be more an index of the mother's disease than of its own. Sylvester, Jeans and Cooke wait 8 weeks before they feel that the serologic test on the infant is indicative of syphilis; a 6-week period was accepted in this study. According to Denny and Pakula, any repeatedly positive serologic reaction appearing in the newborn which lasts more than 3 weeks should be regarded as positive evidence of syphilis. If all findings are negative, the blood should be examined at the third, sixth, ninth, and twelfth months, and thereafter twice a year for the first 5 years or longer. It is the author's opinion that the period of observation should extend to or beyond adolescence. She cites the case of a child in a family of syphilitics who was repeatedly negative until he was 9 years old, at which time he had a positive Wassermann reaction.

After examining several hundred placentas, the author found in the placentas of nonsyphilitic mothers the same pathology which had been previously considered diagnostic of syphilis. The diagnosis of syphilis of the placenta must rest upon the isolation of the spirochete.

X-ray of the long bones has proved unsatisfactory to the author.

**The aetiology of post-arsphenamine jaundice.** J. Beattie and J. Marshall. Brit. M. J., London, No. 4346: 547-550, Apr. 22, 1944.

The authors distinguish between two types of hepatitis which occur during arsenical therapy: (1) An early type which is usually mild and appears within the first 2 weeks after the first injection of the drug, and (2) a late type which may appear at a variable time after starting treatment, but usually becomes obvious between the twelfth and seventeenth weeks of treatment.

The type seen by the authors is the late or delayed form of jaundice which occurs in patients suffering from early syphilis who are being treated with neoarsphenamine by the routine British Army method, that is, 0.6 gm. neoarsphenamine weekly for 10 weeks, followed by an interval of 4

weeks after which a similar second course is given. Third and fourth courses are given, but a 4 weeks' rest period is interposed between each 2 treatment courses. They observed 119 cases of jaundice in men on treatment for early syphilis. In this group, 90 (76 percent) developed jaundice between the twelfth and seventeenth week following treatment, 20 as late as the forty-fourth week, and 9 before the twelfth week.

From their observations, the authors conclude that infective hepatitis has an incubation period of about 28 to 30 days and is transmitted by contact. It can exist in a form in which icterus never appears but which is apparently sufficient to confer immunity against reinfection. Late postarsphenamine jaundice or homologous-serum jaundice has an incubation period of 80 to 100 days and is transmitted by inoculation of infective agent, such as blood, serum or plasma. It seems that the one disease does not form an immunity against the other, but relapses of late postarsphenamine jaundice seem to be due to infective hepatitis.

It is not known whether an attack of postarsphenamine jaundice due to inoculation with icterogenic serum or plasma will give immunity against infective hepatitis occurring during arsphenamine treatment for syphilis.

In conclusion, the authors state that in view of the identity of clinical, biochemical and pathologic pictures of infective hepatitis and late postarsphenamine jaundice the final proof of the reality of two infective factors must rest in the end on the production of convincing serologic evidence and the accumulation of more data on their etiology.

**Lupus erythematosus with false positive Kahn reactions.** Lauren Sompayrac and Hugh E. Hailey. Arch. Dermat. & Syph., Chicago, 49: 355, May 1944.

A 23-year-old enlisted Navy man, apparently in good health at the time of enlistment, reported to sick bay 5 months later complaining of painful feet. The Kahn reaction upon admission was positive, but although no antisyphilitic treatment was

given it reverted to negative 23 days later, at which time all pain had subsided. He was hospitalized a month later for metatarsalgia, anorexia and lassitude. At this time the Kahn reaction was doubtful, but reversed to negative in a week. Rest in bed relieved these symptoms and he was returned to duty. Seven months after the first symptoms he developed lupus erythematosus on each cheek, which was treated by local applications. Six months later he was again hospitalized for myositis at which time the Kahn reactions were positive on three different occasions. He was given antisyphilitic treatment, but after 3 injections of neoarsphenamine, nausea and vomiting occurred followed by dark hemorrhagic lesions of lupus erythematosus on his neck and a return of the lesions on his face. There was an acute exacerbation of pain in his feet, with swelling and tenderness of the ankles and wrists. This condition persisted for 1½ months when he showed some improvement and the Kahn reaction was doubtful. He was discharged to light duty 1 month later. The Kahn reaction remained negative.

It is believed that this patient had symptoms of lupus erythematosus before the appearance of cutaneous lesions.

**Syphilis and tuberculosis.** (Lues und Tuberculose.) E. Köhler. *Deutsches Tuberk.-Bl.*, Leipzig, 17: 166-168, 1943.

At the Moltkefels Sanitarium the Meinicke opacification test (M.T.R.) for syphilis has been used routinely since 1926 in the examination of tuberculous patients on their admission to the sanitarium. Among 8,425 tuberculous men 173 (2.05 percent) were found to be syphilitic; 62 had open tuberculous lesions and 111 had closed lesions; 26 had repeated admissions to the sanitarium, making it possible to observe them for periods up to 15 years. Only 1 of these 26 patients who were observed over a long period of time showed definite improvement of his pulmonary tuberculosis. This patient, as well as a large number of the 173 diagnosed as having syphilis, did not receive antisyphilitic treatment because there were no other findings of syphilis

outside of the positive Meinicke reaction. (According to E. Hoffmann persons with positive serologic reactions but no subjective or objective findings of syphilis should not be treated.) In cases of active syphilis the dose of 0.45 gm. neoarsphenamine was not exceeded. With the possible exception of tertiary syphilis, syphilitic infection was not found to have an untoward effect on the healing of the tuberculous involvement.

**Transmission of gonorrhea through buccal coitus.** Samuel D. Allison and Bernard Witlin. *Clinical Notes. Hawaii M. J.*, Honolulu, 3: 176-177, Mar.-Apr. 1944.

Three cases of gonorrhea acquired through buccal coitus have been reported to the Hawaii Board of Health. In each case typical gram-negative diplococci were found, cultures of which produced oxidase positive colonies. In order to biochemically substantiate the classification of these oxidase positive colonies of gram-negative diplococci as *Neisseria gonorrhoeae*, transplants were made to the various sugars and in every instance fermented glucose, but did not ferment lactose, sucrose, maltose, levulose or mannite. Since these patients were treated by private physicians, the method of treatment is not known; but from the examinations all responded promptly.

As these cases were discovered by contact examination, it is advisable to question the patient with gonorrheal urethritis as to the type of sexual contact—vaginal, buccal or rectal—and the contact should be examined at the appropriate site of exposure.

**An epidemic of genital chancres from perversion.** Herman Goodman. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, 28: 310-314, May 1944.

An outbreak of genital chancres was seen in a group of 18 male youths ranging from the ages of 17 to 28 years. Homosexual exposure among the group was confirmed. Eight of the number and the alleged source of infection (a 28-year-old unmarried white man) were found to be infected. The remaining 9 showed no evidence of syphilis after 3 months' observation.



Sixteen of the youths were examined at the Williamsburgh-Greenpoint Social Hygiene Clinic of the Bureau of Social Hygiene and 2 at Bellevue Hospital. Forty familial contacts and 2 nonfamilial female contacts examined at Williamsburgh-Greenpoint Clinic were negative. No primary oral or anal lesions were found and it is believed that only those practicing homosexuality were infected.

All of the infected cases were given intensive antisyphilitic treatment, with satisfactory results.

**Relationship of lymphogranuloma venereum infection to the incidence of hyperglobulinemia.** Paul B. Beeson and Edward S. Miller. *Am. J. M. Sc., Philadelphia*, 207: 643-647, May 1944.

Because of the prevalence of lymphogranuloma venereum in the Negro population in Georgia, a study was made of the incidence of hyperglobulinemia in 2,375 serums from both white and Negro population. The formol-gel test was used to detect the presence of increased globulin. Hyperglobulinemia was found in 0.4 percent of white males and in 0.6 percent of white females; in Negroes the rates were 5.6 and 8.3, respectively. The difference in prevalence of lymphogranuloma venereum is presumed to be the explanation of this racial difference. Of 125 serums from Negroes, 74 gave a positive test for lymphogranuloma venereum. In these two groups there were 13 cases of hyperglobulinemia; 12 of them were from persons with lymphogranuloma venereum, while only 1 was from a person with syphilis alone. This points to lymphogranuloma venereum rather than to syphilis as the principal cause of hyperglobulinemia.

**The incidence and significance of *Trichomonas vaginalis* infestation in the male.** Louis G. Feo. *Am. J. Trop. Med., Baltimore*, 24: 195-198, May 1944.

The author, who was assigned to the Genito-Urinary Section of the Station Hospital at Fort George G. Meade, Md., had the opportunity from September 1942 to March 1943 of examining admissions for the presence of *Trichomonas vaginalis*.

Urethral specimens were provided by 926 men (735 Negro, 191 white). Identification of the organisms was by means of microscopic examination of the moist films, made either immediately or within 2 hours after collection.

Of the 735 Negroes examined, 407 (55.37 percent) were positive for gonococcus and 121 (16.46 percent) showed *Trichomonas vaginalis*. Only 18 (2.45 percent) of the 735 men showed both the gonococcus and *Trichomonas vaginalis*. Of the 191 white men examined, 110 (57.59 percent) were positive for the gonococcus, 23 (12.04 percent) showed *Trichomonas vaginalis*, and 1 showed both gonococcus and the flagellate.

Of the 926 men examined, 246 (26.5 percent) were classified as having nonspecific urethritis. The incidence of *Trichomonas vaginalis* found in this group was 28.7 percent in the white men and 39 percent in the Negro.

Of the 144 trichomonad positive cases there were 24 (8 white, 16 Negro) which gave persistently positive spreads containing numerous trichomonads and bacteria, similar to those seen in cases of *Trichomonas vaginalis* vaginitis.

The urethral discharge of the 144 trichomonad positive group was slight in amount, varying from a watery, flecked with white, type to one that was greyish-yellow in color, and thin in consistency. The microscopic examination revealed few epithelial cells, few to moderate numbers of leukocytes and bacteria, with few motile trichomonads.

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## TREATMENT

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**Experimental prophylaxis and treatment of chancroidal infection: Inefficacy of penicillin administered intramuscularly.** Armand J. Pereyra and Simeon Landy. *U. S. Nav. M. Bull., Washington*, 43: 189-191, July 1944.

A study was made on the effect of penicillin treatment in experimentally produced chancroidal infections in the human. Mul-

multiple chancroidal infections were produced in the skin of the thighs of 3 patients being treated with penicillin for other conditions. The inoculum was prepared from freshly isolated strains of *Haemophilus ducreyi*. Lesions appeared in from 3 to 5 days.

The first patient was inoculated at 8 sites on the thighs, and treatment, consisting of a total of 600,000 units of sodium penicillin, was begun on the following day. The lesions evolved rapidly and were well developed by the fourth day. At the time of inoculation of the second patient penicillin had been given for 14 days, and was continued for 2 more weeks. Typical chancroidal infections developed at the site of each of the 4 inoculations within 5 days. In each of these patients the lesions developed more rapidly and more extensively than those in patients similarly inoculated but not receiving penicillin. Penicillin was given to the third patient for 14 days following inoculation, and the chancroidal lesions developed rapidly.

From these experiments, sodium penicillin was found not to be effective in preventing or in curing the experimental chancroidal infection of the skin in the human in dosages of from 5,000 to 10,000 units given intramuscularly every 3 hours. The rapid development of chancroidal lesions in these patients indicates that penicillin facilitates establishment of chancroidal infection, possibly by a lethal effect upon susceptible contaminants. In all 3 of the cases the lesions responded to treatment with sulfathiazole.

These findings suggest that penicillin resistant chancres might be due to a mixed infection with *H. ducreyi*. The presence of these organisms in such a lesion would require supplementary treatment with sulfonamides.

#### **Studies on the action of penicillin. I.**

**The rapidity of its therapeutic effect on gonococcic urethritis.** C. Phillip Miller, William Wallace Scott and Velma Moeller. *J. A. M. A.*, Chicago, 125: 607-610, July 1, 1944.

Twenty-one patients with gonococcic urethritis, including early acute and chronic

sulfonamide resistant infections, were treated with penicillin and the action of the drug studied. The penicillin was administered by injection of 1 or 2 cc. of aqueous solution into the gluteal muscles. Sterile, pyrogen-free water was used for its solution. The dosage ranged from 50,000 to 100,000 Oxford units, varying the size and spacing of the individual injections, in most instances over a period of 5 hours or less. No toxic reactions resulted in any of these patients.

With 1 exception, in every case the urethral exudate underwent a striking change in character and quantity within 2 or 3 hours after the initiation of treatment and before the course of injections was complete, and within 5 or 6 hours the infection had practically disappeared. Stripping the urethra produced a small drop of clear watery secretion, but the following morning no discharge was apparent and none could be produced by stripping the urethra. Also local tenderness and pain on urination were relieved. Through an error, the 1 patient who had not responded to treatment had received a smaller dose of penicillin than was intended, which resulted in the persistence of the urethral discharge. However, this case responded to a second course of 100,000 units.

The first 7 cases were hospitalized for treatment but the remainder were treated in the outpatient clinic, where they were kept under supervision during the period of treatment and observation. The latter method proved equally successful in all cases. In 2 cases the penicillin was administered by urethral instillations without success, but responded to intramuscular injections.

**Penicillin in the treatment of ophthalmia neonatorum.** Jerome J. Sievers, Leslie W. Knott and Herman M. Soloway. *J. A. M. A.*, Chicago, 125: 690-692, July 8, 1944.

During the past several years 35 infants with ophthalmia neonatorum have been treated with the sulfonamides by the Illinois Department of Public Health. Although no blindness has resulted among



these cases, many infants were either intolerant to the sulfonamides or quickly became resistant; prolonged hospitalization was also usually necessary. Therefore when penicillin became available its effect on ophthalmia neonatorum was studied. Eight cases have been treated with intramuscular injections of penicillin in total dosages varying from 60,000 to 330,000 units.

In 5 of the 8 cases the etiologic agent was definitely established as *Neisseria gonorrhoeae* by confirmatory fermentation tests. In 2 of the cases gram-negative intracellular diplococci gave positive oxidase reactions when grown on chocolate agar but could not be subcultured for confirmatory fermentation tests, and in 1 case the infective agent could not be determined.

Six of the 8 cases responded promptly to penicillin, with pronounced clinical improvement within 24 hours and complete recovery within 3 to 6 days. The disappearance of specific organisms in spreads and cultures was noted in from 9 to 24 hours after beginning treatment with penicillin.

A possible reaction to penicillin was observed in one case, the child developing a generalized papular eruption; however, periodic allergic manifestations continued after the penicillin was stopped.

**Results of penicillin treatment of sulfonamide-resistant gonorrhea: Summary of 4,439 cases treated in United States Naval Hospital July 1943-March 1944.** Walter H. Schwartz and Cary O. Edge. *U. S. Nav. M. Bull.*, Washington, 43: 193-195, July 1944.

The results of penicillin treatment of 4,439 cases of sulfonamide resistant gonorrhea seen in U. S. naval hospitals for the period July 1943 to March 1944 are summarized.

Of 4,439 cases of sulfonamide resistant gonorrhea treated with penicillin, 4,258 (95.92 percent) were reported as successfully cured by the first course of therapy, 139 were retreated successfully, 2 were definitely failures despite retreatment, and 40 were reported as failures but were not retreated.

The method of administration in the majority of cases was either intramuscularly or intravenously. The total dosage varied from 125,000 units intramuscularly prior to November 1943 to 71,000 units in February 1944, with an average of 99,000 units per case over the entire period. The average intravenous dosage varied from 171,000 units prior to November 1943 to 71,000 units in February 1944, with an average of 152,000 units per case for the entire period. The number of cases requiring retreatment increased with the decrease in the average dosage.

The results in these cases indicate that the intramuscular administration of 20,000 units of penicillin every 3 hours for 5 doses is the preferred treatment of sulfonamide resistant gonorrhea. Retreatment with penicillin is indicated in those cases failing to respond to the first course of penicillin therapy. Dosage schedules used in retreatment are being standardized.

**Concentration of arsenic in blood after administration of mapharsen by rapid drip method: Clinical and experimental studies.** Oswald M. Gruhitz, J. A. Sultzberger and Loren W. Shaffer. *Arch. Dermat. & Syph.*, Chicago, 49: 321-326, May 1944.

Previously studies have been made on the slow continuous drip method of administration of mapharsen used by Leifer, Chargin and Hyman and the rapid or syringe method by Thomas and Wexler in an effort to evaluate these methods in relation to the concentration of arsenic in the blood. This is a report of similar studies in which Shaffer's 1-hour rapid continuous drip method was used for comparison with the other two methods of administration.

Each patient was given 1.2 mg. mapharsen per pound of body weight (2.5 mg. per kilogram) to a maximum dose of 180 mg., dissolved in 1,000 cc. of a 5 percent solution of dextrose. Administration was by gravity, requiring 60 to 75 minutes, and repeated daily for 5 days. The patients were young male and female adult persons, both white and Negro.

The patients were divided into 4 groups. From one group blood for determinations of arsenic was drawn in 10 cc. amounts by syringe from the opposite arm, immediately after treatment. From each of the other 3 groups blood was taken 1, 6, and 24 hours respectively after treatment, following the first, the third, and the fifth treatment. The arsenic content of the blood varied in different patients from about 59.7 to 127.8 micrograms per hundred grams of blood immediately after completion of administration to 24 to 68 micrograms 1 hour after administration, 5.8 to 34.5 micrograms 6 hours after administration, and 4 to 20 micrograms at the end of 24 hours after administration. There was an average range of from 78.6 to 106.2 micrograms of arsenic per hundred grams of blood. The level rapidly decreased as the sampling period was delayed, and in 24 hours it reached a low level of 6.86 micrograms after the first injection and of 16.84 micrograms after administration of the fifth daily dose. The weight, sex, race, daily dose and finding of each patient are tabulated.

Experiments in dogs given equivalent doses by the 1-hour rapid continuous drip and the rapid syringe methods resulted immediately after administration in concentrations of arsenic respectively of 112.4 and 375.5 micrograms per hundred grams of blood, or a ratio of 1:3.3, the latter method giving a concentration three times higher than the former. The arsenic content decreased rapidly with delay of sampling for 1, 3, 6 and 24 hours after administration of mapharsen by either method.

No constant level of arsenic in the blood was found in either clinical patients or dogs. Both patients and dogs reached about the same level of concentration 1 hour after administration, irrespective of the method of administration. Mapharsen rapidly disappeared from the peripheral blood stream after the rapid drip method, the highest concentration being immediately after administration.

The 1-hour rapid continuous drip method of administration of mapharsen caused a slight rise in the arsenic level of the blood

stream after administration of 5 successive daily doses. There was no cumulative retention of arsenic in the blood stream in this group of patients.

#### **Intensive ambulatory therapy of syphilis:**

**Thirty day mapharsen technic.** Samuel Goldblatt. Arch. Dermat. & Syph., Chicago, 49: 403-407, June 1944.

The author reports the clinical observations and laboratory investigations on an unselected group of 107 patients (104 men and 3 women) with syphilis of all types who received intensive arsenical therapy. This consisted of 1,800 mg. of mapharsen, administered in daily doses of 60 mg. for 30 consecutive days.

The serologic reactions, which were positive in 81 percent of the total group before treatment, showed a decided and continuing reduction in titer. On termination of treatment positive serologic reactions were noted in 55 percent, 1 month later in 40 percent, and 2 months later in 35 percent of the patients; from 3 to 6 months after termination of treatment the reactions of 20 percent remained positive. The reactions of an additional 8 percent were reported as doubtful. All patients who began treatment with a negative reaction retained that status during the 6 months of observation. During this period 3 patients had serologic relapses, as shown by an increase in titer; retreatment was carried out on them.

The spinal fluids of 9 patients gave positive reactions originally; 6 became negative and 3 remained persistently positive. No significant changes were noted in the blood and electrocardiographic examination indicated no toxic sequelae.

A sulfonamide in 6 gm. daily doses was given concurrently to 40 patients for treatment of an associated gonorrhea, chancroid or lymphogranuloma venereum. Alcoholism did not contraindicate the intensive treatment. Complete healing of all the lesions of infectious syphilis required an average of 10 days. There were 2 cases of Herxheimer reaction and 2 simulating ninth day erythema.

The clinical value of this therapy cannot be finally estimated for some years.



**Sulfarsphenamine in the therapy of syphilis. A comparative study of the toxic manifestations of neoarsphenamine and sulfarsphenamine.** Thomas F. Probey, Edgar W. Norris, Austin V. Deibert and Eleanor V. Price. Pub. Health Rep., Washington, 59: 733-752, June 9, 1944.

The authors review the literature on the toxic manifestations of the arsphenamines, covering 33 references. From their observations and the continued satisfactory reports of the U. S. Navy Medical Services it appears that a reinvestigation should be made on the toxicity of sulfarsphenamine. They found no more toxic than neoarsphenamine, the greater stability and ease of administration of sulfarsphenamine should increase its utilization in antisyphilitic therapy.

The clinical facilities of the U. S. Public Health Service at Hot Springs, Ark., were made available for a reinvestigation of sulfarsphenamine, which was begun in January 1940 and continued for 18 months. During this period 16,878 intravenous injections of arsphenamines were administered, — 9,148 of neoarsphenamine and 7,730 of sulfarsphenamine. Approximately one-eighth of the patients had mixed infections of gonorrhea and syphilis.

The reaction rate for neoarsphenamine (minor 43.9, major 7.2 per 1,000 injections) was only slightly less than that for sulfarsphenamine (minor 49.2, major 7.8 per 1,000 injections) and is of no statistical significance. These results are higher than the reaction incidence reported by the Co-operative Clinical Group for the same drugs.

Sulfarsphenamine was found to be particularly toxic in white females, the rate of major reactions being 17.2 per 1,000 injections and more than twice that in white males; it was more than 60 percent greater than the highest rate of major reactions following neoarsphenamine (10.5 per 1,000 injections in white males).

The minor reactions following neoarsphenamine were gastrointestinal (26.8 per 1,000) and febrile (6.0); following sulfarsphenamine, gastrointestinal (26.6), slight skin eruption (7.6) and pruritus

(5.7). The major reactions following neoarsphenamine were icterus (3.3) and dermatitis (2.6); following sulfarsphenamine, dermatitis (3.1) and purpura haemorrhagica (2.9).

When sulfonamide was administered concurrently with sulfarsphenamine the incidence of purpura haemorrhagica (6.1) was two and one-half times more frequent than when sulfarsphenamine (2.4) was administered alone, while administration concurrently with neoarsphenamine did not influence the reaction rates.

In the first course of therapy, sulfarsphenamine is less toxic; in the second and third courses, neoarsphenamine.

Laboratory investigations indicate that sulfarsphenamine is definitely more stable than neoarsphenamine and apparently more active treponemically. On the basis of animal experiments, it is suggested that sulfarsphenamine may be clinically more effective than neoarsphenamine.

**Studies on the prevention and treatment of experimental renal obstruction from sulfadiazine.** David Lehr. Bull. New York Acad. Med., New York, 20: 424-425, July 1944.

Evaluation studies were made on the prevention and treatment of experimental renal obstruction from sulfadiazine. Albino rats were fed water and for alkalization, sodium bicarbonate, and for purposes of comparison 2 subgroups were fed solutions containing an acidifying salt (sodium chloride and ammonium chloride). Repeated injections of sodium sulfadiazine were given all rats, in amounts which were known to produce invariably massive precipitation of sulfadiazine in the renal tubules, provided no therapy was employed. Postmortem examinations were performed on all animals and the organs studied histologically.

Chronic sulfadiazine intoxication was found to produce in rats severe changes in the kidneys, the aorta, the arteries, and the thyroid gland. The kidneys showed massive intratubular precipitation of sulfadiazine accompanied by severe tubular dilatation and degeneration of the parenchyma. The aorta showed necrosis of the media, and the thyroid gland, enlargement associated

with the histologic picture of high glandular activity.

The investigation proved that in the animal experiment intrarenal concrement formation from sulfadiazine and its serious consequences can be prevented by alkalization in conjunction with the "forcing of water." It was found, however, that forcing of water alone, as well as the administration of acidifying salt solution, did not provide adequate protection.

Treatment of renal obstruction consisted of stomach tube feedings of fixed amounts of water or salt solutions (containing either  $\text{NaHCO}_3$ ,  $\text{NH}_4\text{Cl}$ , a mixture of these two, or  $\text{NaCl}$ ). The fluids were given twice daily, starting with the day of renal obstruction and continuing for at least 1 day. The most striking result was obtained by the use of solutions of  $\text{NaCl}$  and of the mixture of  $\text{NaHCO}_3$  and  $\text{NH}_4\text{Cl}$ . They made possible the recovery of all rats from an otherwise fatal sulfadiazine intoxication, whereas no benefits were derived from the "forcing of water" alone.

It is therefore seen that the combination of the alkalizing and acidifying salts in one solution will prevent changes in the acid-base balance of the body, thus allowing the increased crystalloid concentration to initiate a powerful diuresis. This also explains the value of large doses of saline solution.

**Surgical treatment of the rectal stage of lymphogranuloma venereum: Abdominoperineal transanal resection with perineal colostomy and preservation of the anal sphincter. Report of cases.** J. Noya Benítez and Luis R. Gúzman López. Puerto Rico J. Pub. Health & Trop. Med., New York, 19: 428-453, Mar. 1944.

The authors review the literature on lymphogranuloma venereum, covering the various methods of surgical treatment given in rectal strictures. A total of 35 references are cited.

A modification of the Babcock technic, a one-stage combined abdominoperineal resection with perineal anus and conservation of the sphincter ani, is the method favored by the authors. At present they have treated 12 patients with stricture of the rectum by

this method without a fatal result. A detailed description of the operation is given.

An analysis is given of 9 of the cases treated. The youngest patient was 25, the oldest 48 years old; 8 female (5 Negro, 3 white) and 1 male (white). The rectal symptoms had persisted from  $1\frac{3}{4}$  to 11 years. One woman gave a history of primary lymphogranulomatous lesion, 2 women had had inguinal buboes several years previously, and the man had had buboes 12 years previously. The most general symptoms seen were severe constipation, ribbon stools, and profuse, purulent rectal discharge both during and between defecation. One female patient gave a positive Kahn reaction.

All the authors' cases have been followed up from 2 to 17 months. However, the authors feel that these follow-up periods have not been sufficiently long to consider the patients as totally cured and only prolonged observation will determine whether recurrences are apt to occur.

A brief summary of the 3 additional cases is given.

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## PATHOLOGY

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**Renal pathology following the use of sulfa drugs.** Eunice S. Greenwood Kentucky M. J., Bowling Green, 42: 174-178, June 1944.

When selecting the type of sulfonamide to be used, consideration must be given to (1) the amount of acetylation of the drug which occurs in the blood, tissues and urine, (2) the solubility of the drug and its acetylated form in the tissues, (3) the amount of reabsorption from the kidney, both of the drug and its acetylated form, (4) the rate of excretion, (5) the tendency of the drug to cause acidosis, and (6) the solubility of the drug in a concentrated aqueous solution or buffered aqueous solution of varying pH as found in the urine. These facts combined with the amount of drug needed to produce bacteriostasis give the clue to the efficacy and development not only of complications but also of the type



of complication, and therefore give the clue to remedial measures or treatment. This knowledge also forms a basis for the development of new drugs.

The only toxic conditions resulting from the use of sulfapyridine, sulfathiazole, sulfadiazine and sulfamerazine, which have a bearing on renal pathologic changes, are hepatitis and acute hemorrhagic anemia. Most patients who have severe liver damage develop an associated nephrosis. The complications of hepatitis and acute hemorrhagic anemia have greatly diminished in the last 3 years.

In addition to mechanical damage large collections of crystals of the acetylated or free drug can produce obstruction with resulting anuria. The author believes accumulations of sulfonamide crystals are not opaque, but if calcium is added a shadow on the roentgenogram might be expected. The author cites a case in which such a shadow was seen in anuria due to a block by sulfadiazine in the pelvis of the kidney. After ureteral lavage and removal of the block the shadow disappeared. This patient had a preexisting pyelitis. In one case reported in the literature a large mass, part of which proved to be sulfapyridine, was surgically removed from the renal pelvis 2 years following sulfapyridine therapy. In another case surgery was necessary for a fibrinopurulent membrane with calcium deposit and mixed sulfonamides.

Sulfamerazine has been found to combine minimum dose, maximum solubility in acid or alkaline solution, maximum reabsorption from the kidney, maximum solution in blood and tissues, and least conjugation. With the introduction of this drug is expected minimum toxicity plus minimum renal damage.

**The pathologic changes produced by prolonged administration of sulfapyrazine and sulfamethyldiazine (sulfamerazine) in the kidneys of rabbits as compared with sulfathiazole and sulfadiazine.** Fritz T. Callomon. *J. Lab. & Clin. Med.*, St. Louis, 29: 574-584, June 1944.

The authors describe in detail their experiments in their study of the extent and site of pathologic changes produced in the

kidneys of rabbits by the prolonged oral administration of sulfapyrazine and sulfamerazine as compared with sulfathiazole and sulfadiazine. They found that sulfapyrazine and sulfamerazine, when given in doses of not more than 0.05 or 0.1 gm. per kilogram twice a day for 10 days in succession (20 doses), did not produce marked tissue damage in the kidneys of rabbits, except for an occasional focus of tubular epithelial necrosis in a few areas. The same results were obtained with sulfathiazole and sulfadiazine. All rabbits in the experiments receiving doses of 0.05 or 0.1 gm. per kilogram survived.

When doses of 0.2 or 0.25 gm. per kilogram were given, all compounds showed nephrotoxic effect in varying degrees.

Sulfathiazole in dosage of 0.2 gm. per kilogram produced a lesser degree and lesser extent of kidney damage than did the other compounds. Sulfapyrazine produced less kidney damage than did sulfadiazine or sulfamerazine.

Sulfamerazine, in doses of 0.2 or 0.25 gm. per kilogram, showed great ability to cause the formation of gross intrarenal and extrarenal concretions (uroliths) as observed in 5 of 6 rabbits. This was not observed with sulfapyrazine and sulfathiazole at equal dosage and only in 2 of 6 rabbits with sulfadiazine, where the extrarenal concretions in the renal pelvis were small and scarce.

**Meningeal and vascular syphilis of the spinal cord.** Raymond D. Adams and H. Houston Merritt. *Medicine*, Baltimore, 23: 181-214, May 1944.

The authors classify and discuss spinal syphilis, based on pathologic changes, as (1) syphilitic meningomyelitis; (2) spinal vascular syphilis; (3) syphilitic spinal pachymeningitis, (a) gumma of spinal cord, (b) syphilitic hypertrophic pachymeningitis; (4) syphilitic poliomyelitis. As a basis for their study, the anatomy and physiology of the spinal cord are reviewed. A pure form of spinal syphilis without lesions of the brain is exceptional; usually there is pathologic evidence of involvement of several portions of the neuraxis. Probably the basic pathologic lesion is

chronic inflammation of the spinal meninges, a chronic spinal leptomeningitis. In an intense syphilitic infection of the meninges and spinal cord a gumma may form. Since there is the combination of chronic meningitis, arterial disease and granuloma formation, it is not surprising that almost every conceivable cord disease may be simulated clinically by spinal syphilis. No one of these pathologic reactions is absolutely pathognomonic of syphilis, but taken as a group they are highly characteristic.

Syphilis of the spinal cord is a clinical rarity. There were 31 cases among 2,231 syphilitic patients at the Boston City Hospital. The majority of the patients were in the fifth decade of life; over two-thirds had received no antisyphilitic treatment and the remainder inadequate treatment.

There were 15 cases of syphilitic meningomyelitis. The principal symptoms and signs in this manifestation are paraparesis or paraplegia, urinary and fecal incontinence and sensory disorders. Both legs are usually involved simultaneously in the invariable weakness or stiffness. The gait may be that of ataxic paraplegia. The sphincters are nearly always involved.

There were 16 cases which could be included under spinal vascular syphilis, 6 of them occurring after some treatment procedure. The authors believe that the introduction of any foreign substance intrathecally, whether for spinal anesthesia or arsphenamized serum, in a patient who already has neurosyphilis is fraught with considerable danger.

Syphilitic spinal pachymeningitis was found in 4 of the cases; in 3 there was a gumma and in 1 diffuse inflammation and thickening of the dura. The 3 patients with gumma were operated upon, but all died within 9 months.

Ten of the cases are discussed at length.

In a high percentage of the cases the blood and cerebrospinal fluid were both abnormal, particularly in the active cases. With the exception of 1 questionable case, in none of the cases were both the cerebrospinal fluid and blood reactions negative.

The clinical diagnosis of syphilitic meningomyelitis may baffle even the most expert. The various neurologic syndromes associ-

ated with alcoholism and multiple vitamin deficiencies often add to the difficulty of diagnosis. Pachymeningitis and spinal gumma are confused only with tumor or spinal tuberculosis.

The clinical results in treatment of spinal neurosyphilis are discouraging. The follow-up data on the authors' cases are too meagre to be of use. The authors doubt whether malarial therapy is ever indicated. Anterior rhizotomy may be used in cases where flexion attitudes and flexor spasms are present.

**Deaths from sulfonamides: A clinical and pathological study, with a report of three cases.** C. N. Gessler. *South. M. J.*, Birmingham, 37: 365-372, July 1944.

The pathologic findings in 3 cases of death from administration of sulfonamides are presented. The major cause of death in these cases was uremia, but in 1 case a previously undescribed type of pulmonary pathologic change was believed to be an important factor. This case, a 24-year-old white male, had been treated for a gonococcal infection with gonococcus vaccine and sulfathiazole. He had appeared to be well until the development of the urethral discharge 2 weeks prior to admission. He was given 3 injections of gonococcus vaccine and 8 gm. of sulfathiazole daily for 3 days and then 6 gm. daily for 5 days. The discharge cleared up on the fifth day of treatment. He then developed chills and fever followed by an itchy erythematous rash and pain in the lower lumbar region. He was hospitalized at this time. Treatment consisted of intravenous hypertonic glucose, intravenous aminophyllin and sedation. He remained anuric, passed bloody urine and steadily grew worse and died 5 days after admission. Postmortem findings and examination of microscopic sections showed acute tubular nephritis, acute interstitial pneumonitis, acute interstitial myocarditis, infarct of kidney, focal necrosis of liver and kidneys, and acute splenitis.

Thirty cases from the literature are reviewed and analyzed, and the mechanism of production of the pathologic lesions is discussed in this report. The particular dr



the sulfonamide group used seemed to have little bearing on the type or severity of the complicating toxic manifestations. Anemia and agranulocytosis are the most frequent lethal complications. Although sulfathiazole is apparently the cause of these reactions more often than any other drug, it was used in some cases. A list of 41 references is included.

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## LABORATORY RESEARCH

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**Simplified technique for the agar cup assay of penicillin.** Louis S. Cholden. J. Bact., Baltimore, 47: 402-403, Apr. 1944.

A simplified technic for the agar cup assay of penicillin is given which is especially adaptable to laboratories that do not have the extensive apparatus necessary for the usual cup assay procedures, and where mass production methods are not essential. The organism which has been found to be the most satisfactory for the test is a staphylococcus aureus (Norsenski), or any of its strains can be used which are found not to give zones of partial inhibition and secondary zones of stimulation.

A detailed description of the method is given.

**The combined antimicrobial activity of urea and sulfathiazole in urine.** Erwin R. Neter and Phyllis Clark. J. Urol., Baltimore, 51:101-109, Jan. 1944.

The authors carried out experiments to determine whether or not (1) urea in urine exerts bacteriostatic and bactericidal activity and (2) urea and sulfonamides act synergistically in urine against microorganisms commonly encountered in infections of the urinary tract.

Their conclusions were that normal human urine supports the growth of *B. coli*, *S. aerogenes*, *B. alcaligenes*, *B. proteus* and *S. morganii*. Urea in urine in concentrations ranging from approximately 3.6 to 6.7 percent either definitely delays the growth of these organisms or prevents it com-

pletely. Urea and sulfathiazole in urine, when used simultaneously, act synergistically and produce greater bacteriostatic and bactericidal effects toward *B. coli* and greater bactericidal effects toward hemolytic streptococcus group A than either drug alone in like concentrations or in concentrations  $1\frac{1}{2}$  to 2 times as great.

**Use of liver extract as an enrichment factor for the growth of gonococci.** E. Altire-Werber. J. Bact., Baltimore, 47:399-400, Apr. 1944.

It has been found that aqueous solutions of liver extract powder  $1/25$  (Armour) could be used as an enrichment in gonococcus culture mediums in place of fresh liver preparations. This product represents the aqueous extract of fresh liver dried in vacuo at a low temperature. Processing does not seem to affect the thermolabile factor necessary for the growth of certain strains of *Neisseria gonorrhoeae*. This liver extract alone or in combination with citrated hemolyzed horse blood proved to be a suitable adjuvant to mediums used for the cultivation of gonococci.

The method of preparing the various mediums is given.

**Gonococcus cultures—A State laboratory service.** Margaret W. Higginbotham. Am. J. Pub. Health, New York, 34: 643-647, June 1944.

An attempt was made to find a satisfactory method for shipping gonococcus culture specimens to the laboratory for examination. The Division of Preventable Diseases of the Minnesota State Department of Health has found the following method to be serviceable and convenient: The material for culture, collected on sterile swabs, was emulsified in 1 to 2 ml. of fluid in 5 ml. vials. At this time 2 plates of solid medium (McLeod chocolate agar and cystine chocolate agar) were inoculated and a spread was made on a glass slide for microscopic examination. The plates were incubated within 4 hours and were the "control" cultures. The inoculated vials of fluid were placed in a tin container which was then packed in ice in a 1-gallon hot-cold picnic jug and shipped to the laboratory. As

many as 8 specimens were packed in one jug.

Results of a study show that cultures of shipped specimens are superior to microscopic examination of spreads alone for obtaining laboratory evidence of gonococcus infection where facilities for immediate cultures are not available. The examination of cultures of shipped specimens together with spreads yielded almost twice as many positives as spread examinations alone. However, immediate cultures were shown to give double the satisfaction of any other method.

**Culturing the gonococcus.** Arthur M. Kaplan. U. S. Nav. M. Bull., Washington, 42: 1410-1411, June 1944.

The use of penicillin in gonococcal infections has emphasized the importance of culturing *Neisseria gonorrhoeae* for adequate compilation of data in the evaluation of the drug.

A variation of technic in culturing the gonococcus which aids in the successful growth of *N. gonorrhoeae* is given. Sterile human whole blood is added to the agar base prior to the pouring of the plates. The blood used is citrated blood rejected by the blood and plasma bank because of undue cloudiness of plasma. Bacto Proteose No. 3 Agar Dehydrated is the base medium employed. Two hundred cubic centimeters double strength agar, pH 7.3, are prepared, autoclaved at 15 pounds pressure for 30 minutes, cooled to 90° C. in a water bath, and 20 cc. sterile blood is added while the medium is agitated to obtain an even suspension. The agar is cooled to 50°C. in a water bath, poured into sterile Petri dishes in 15 cc. amounts and allowed to harden. The dishes then are inverted and stored in the refrigerator. In order to avoid drying out of the agar the plates should be made frequently.

Cultures are taken before and after the administration of penicillin. Inasmuch as penicillin is indicated in patients whose infection is resistant to the sulfonamides, and thus may be assumed to have received them, it is essential that the possible presence of sulfonamides in the secretions be guarded against to prevent inhibition of

growth of the organism. Primary cultures are therefore taken at a suitable interval after the sulfonamides have been discontinued and prior to the administration of penicillin. Five-tenths milligrams percent of p-aminobenzoic acid may be added to the medium to neutralize the sulfonamides, but prior cessation of sulfonamide therapy is the preferred method. Final cultures are taken 12 to 18 hours after the last dose of penicillin to prevent inhibition of growth by traces of the drug.

When cultures are to be made the chocolate agar plates are warmed in the incubator at 37° C. and sent to the ward where the urethral, prostatic, or conjunctival secretions are streaked directly onto the plate with a sterile wire loop. All cultures are made directly onto the medium. The plates are returned to the laboratory immediately, inverted, and incubated in a moist atmosphere of approximately 10 percent carbon dioxide for 24 to 48 hours. Ten percent carbon dioxide tension is produced through the use of a candle jar; moisture is provided by a small, damp cotton sponge placed in the jar.

For the oxidase reaction a 1 percent aqueous solution of p-aminodimethylaniline monohydrochloride is prepared daily. In the report the results of the "oxidase" reaction and the Gram's stain are included.

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## PUBLIC HEALTH ADMINISTRATION

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**Venereal diseases: Constitutionality of State statute authorizing physical examination of defendant in criminal cause suspected of venereal infection.**  
J. A. M. A., Chicago, 125: 512-513, June 17, 1944.

An Illinois statute provides that, if a person coming before any judge or justice of the peace on any criminal charge is suspected of having any communicable venereal disease, the judge or justice shall cause the defendant to be examined for the presence of venereal disease. If the defendant is found infected, the judge



justice is empowered to commit him or her to an appropriate institution for segregation and treatment. In the present case, the two petitioners were charged with solicitation of prostitution and the justice of the peace ordered them held without bail and examined to determine whether or not they were infected with venereal disease. Both defendants refused to submit to examination and filed petitions for writs of habeas corpus in the city court of East St. Louis, which after a hearing, remanded them to the custody of the chief of police.

The case was carried to the Supreme Court of Illinois. The court held that since the statute is based on the police power of the State and does not fall within the criminal code, it violated no portion of the constitutional provisions that (1) a defendant has the right to be heard in criminal charges and to demand the nature and cause of the accusation, and (2) bail may not be denied to defendant not charged with a capital offense. The petition for a writ of habeas corpus was accordingly denied and the petitioners were remanded to the custody of the chief of police.

**Druggist fined for sulfathiazole sales.** *Med. News. J. A. M. A., Chicago, 125: 219, May 20, 1944.*

The first prosecution of its kind by the Food and Drug Administration was said to have occurred in Portland, Maine, recently when a druggist was found to have been selling loose tablets of sulfathiazole in 100 tablet bottles. In one case a purchaser to whom he had dispensed 50 tablets for self medication had suffered serious consequences. According to the New Hampshire Health News, it is reported the dealer in question was found guilty and sentenced to pay a fine of \$1,000, the latter suspended on a plea of poverty.

**Public health venereal disease control. The private physicians' increasing responsibility. A report of the success of Philadelphia's cooperative plan.** Norman R. Ingraham, Jr., and Sigmund S. Greenbaum. *J. A. M. A., Chicago, 125: 527-530, June 24, 1944.*

A survey conducted conjointly by the

Philadelphia Department of Public Health and the Committee on Venereal and Cutaneous Diseases of the Philadelphia County Medical Society, during the fall of 1943, revealed a definite increase in venereal disease patients receiving private medical care in Philadelphia. Since 1940, the number of syphilitic patients being treated by private practice has increased 86 percent, and gonorrhea 30 percent for the same period. This is the result of increased case finding incident to the war and of increase in the economic status of many of the venereal disease patients seeking medical care.

The active effort to bring about a fuller utilization of private medical practice in the treatment of venereal disease patients consisted in (1) an open appeal to all the physicians in the community to take a more active interest in the management of venereal disease patients; (2) preparation of the "Bulletin of Physicians in Philadelphia who will Accept for Examination and Treatment in Private Practice Patients with Gonorrhea or Syphilis"; (3) a persistent policy on the part of the health department to place under private medical care whenever possible the large numbers of patients disclosed by the enormous amount of current routine serologic testing in industry, by Selective Service examinations, and by the investigation of sources of infection named through the military and other epidemiologic reports; (4) active efforts to bring the most recent authoritative information concerning local venereal disease control problems both to the medical profession and to the lay public. These efforts have resulted in a redistribution of patients and an increased participation in the program by the private physician. There was an increase of 44 percent in the number of physicians known to be caring for gonorrhea and syphilitic patients in private practice and an increase in the average number of patients under the care of a single physician at any one time.

In all areas where this trend of venereal disease patients to seek private medical care is apparent, there is need for development of a mechanism for conducting this interchange in an orderly manner. Otherwise

many patients, some of whom will be public health problems, will be lost in the transfer, and the general public health of the community will suffer.

**2000 Negro health wardens trained for venereal disease control in Florida.** Florida Health Notes, Jacksonville, 36: 110, 123, June 1944.

Negro Citizens' Wartime Health Committees were active last January during the State-wide campaign to control venereal diseases conducted by the Florida State Board of Health. Special schools were provided to instruct leaders in methods of disseminating venereal disease information. More than 2,000 persons attended schools of from 2 to 5 weeks' duration in Panama City, Gainesville and Jacksonville, and more than 1,500 of them finished the course of instruction on the control of syphilis and gonorrhea.

**The organization and purposes of the State-wide Negro Health Committee.** Richard V. Moore. Florida Health Notes, Jacksonville, 36: 107-109, June 1944.

In connection with National Social Hygiene Day, Feb. 2, 1944, a Negro health conference was held at Bethune-Cookman College, with more than 150 Negro representatives present. Community ways and means for controlling venereal diseases were discussed by many authorities. Reports from Negro citizens' wartime health committees organized in Tampa, Jacksonville, Miami and Pensacola were received.

A State-wide Negro Health Committee was formed with the following objectives: (1) To develop through public relations an attitude of interest, on the part of all citizens, based on sound understandings of the general health problems which exist in Florida and to work toward correcting these problems by improving the conditions which have caused them. (2) To teach through education the facts about communicable diseases and the leading causes of illness and death to all groups, using radio, newspapers, literature, and speakers. (3) To promote essay and poster contests that will produce useful literature on com-

munity health problems and motivate high school and college youths toward professional interests in health education. (4) To establish through a health tag sale during National Negro Health Week a scholarship fund to assist a selected student graduating from a Florida Negro college in securing graduate work in health education. (5) To work closely with the Florida State Board of Health and the Florida Tuberculosis and Health Association to further unify the organization by appointing district chairmen who will be responsible to and for local communities. (6) To hold an annual meeting on National Social Hygiene Day.

**Venereal-disease education in the high school: British Columbia's experiment.** H. Cecil Rhodes and Pauline M. C. Campbell. Canad. J. Pub. Health, Toronto, 35: 181-189, May 1944.

The British Columbia Division of Venereal Disease Control in January 1944 participated in an informal round-table discussion on the venereal diseases with a group of high school students 16 years of age and over. The experiment was successful and was tried out on 3 other high schools with equal success. On the basis of these experiences the technique was modified slightly and a brief was submitted by the division to the Minister of Education, outlining the methods used and requesting approval for adoption on a province-wide scale. The approval was granted on the following basis: The division would provide qualified lecturers who would adhere closely to the presentation described in the brief and would make arrangements directly with the individual high schools, and the approval of the school board would be secured by the principal before a lecture could be given at any high school. During the following year 38 high schools, with a total enrollment of 5,000 senior grade students, participated in the special lecture presentation with no unfavorable results.

An outline of the British Columbia program of venereal disease education in the high schools is given, together with its methods of use, the results of the lectures, and



reactions of the students. The results of a questionnaire distributed among 550 students of both sexes in city and rural schools are tabulated.

Although this plan may not provide the ideal answer to the health department or board of education problems, the authors state that in the 2 years in which the plan has been in operation this technic of presenting a comprehensive outline of the venereal disease problem and its solution has been well received. It offers to the progressive health department and school board an immediate opportunity to provide the youth of their community with essential knowledge which may otherwise be denied them.

**A survey of the incidence of venereal diseases in Toronto in 1943.** Gordon Bates. *Canad. J. Pub. Health*, Toronto, 35: 234-240, June 1944.

In cooperation with the Academy of Medicine, the Health League of Canada conducted surveys of the incidence of venereal disease in the city of Toronto in 1929, 1931, 1937 and in the spring of 1943. The reports of 352 physicians and 17 clinics and institutions were included in the survey of 1943.

The total number of cases of syphilis and gonorrhea reported in the city of Toronto in 1943 was 6,342, a rate of 8.7 per thousand population. Of these, 4,747 were cases of syphilis and 1,595 gonorrhea. The previous surveys showed 5,122 (8.4 per thousand population) cases of both syphilis and gonorrhea under treatment in 1929, 6,094 (9.7 per thousand) in 1931, and 6,188 (9.59 per thousand) in 1937. The incidence of syphilis increased from 4 per thousand population in 1929, to 6.5 per thousand in 1943, while gonorrhea dropped from 3.5 to 2.19 per thousand population for the same period. Of the total number of cases under treatment in 1943, 26 percent of the syphilis patients and 46 percent of the gonorrhea patients were treated by the private physician.

The total number of cases of early syphilis reported in 1937 was 373, while in 1943 a total of 995 cases were reported, or an increase of 167 percent.

**Manual on the distribution of communicable diseases and their vectors in the tropics. Pacific Islands Section—Part I.** Edward Philpot Mumford and John Luther Mohr. Suppl. to *Am. J. Trop. Med.*, Baltimore, 24: 1-26, May 1944.

*Granuloma inguinale (ulcerating granuloma, granuloma venereum).*—About 6,000 cases of granuloma venereum were reported treated in Dutch New Guinea in 1923-1926. In 1935 the disease was reported as limited to a region lying on the southeast of Digoel River, including Frederik Hendrik Islands, and extending as far as the Australian boundary. Cases have been reported from northeast New Guinea, New Britain, New Ireland, the Admiralties, the Territory of Papua and Samarai Island, the Solomons, New Caledonia, the New Hebrides and Western Samoa, and Hawaii.

*Lymphogranuloma venereum (climatic bubo, tropical bubo, lymphogranuloma inguinale).*—Climatic bubo has been reported from New Britain in New Guinea Territory, in Samoa, the Carolines, and the Hawaiian group.

*Chancroid.*—Chancroid has been reported from New Britain, New Ireland, the Caroline Islands, the Marshalls, Nauru, the British Solomon Islands Protectorate, Fiji, Western Samoa, and Tahiti. Hawaii had an epidemic of 25 cases during the summer of 1942.

*Gonorrhea.*—Gonorrhea has been reported generally in all parts of the tropical Pacific Islands Section. In some sections it was reported as early as 1903.

*Yaws-Syphilis Complex.*—Yaws and gangosa have been reported widespread in most parts of the tropical Pacific Islands Section. Goundou is reported from New Guinea, New Ireland, the Loyalty Islands, the Solomons and Samoa. Juxta-articular nodules were first noted in New Guinea in 1901; since then they have been reported from Palau, the Solomons, New Caledonia, the Isle of Pines, the Loyalty Islands, Fiji and Hawaii. Syphilis is reported as rare among the natives in most parts of the tropical Pacific Islands. In many places yaws has been erroneously diagnosed as syphilis.

# New Cases of Syphilis and Gonorrhea in States, Territories, Possessions and Panama Canal Zone

Health officers' monthly statement: Reported for the first 11 months of fiscal years 1943-44 and 1942-43

Area	Cases of syphilis and gonorrhea reported for first 11 months of fiscal year below											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital		1943-44	1942-43
	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43		
United States†	426,180	516,256	72,419	77,113	114,887	137,814	188,552	209,732	12,570	15,274	127,986	125,274
Alabama-----	16,205	19,750	1,983	3,063	3,651	5,424	3,951	5,807	349	469	5,967	7,143
Arizona-----	2,596	2,534	643	371	726	580	1,001	1,372	119	119	1,586	1,411
Arkansas-----	9,061	15,770	1,131	1,630	3,065	6,123	3,508	6,344	198	278	4,072	4,411
California-----	31,015	29,506	5,247	4,054	7,143	6,708	17,184	16,799	895	854	33,067	22,411
Colorado-----	3,511	4,758	852	933	1,010	1,181	1,521	2,437	128	207	3,013	2,511
Connecticut-----	2,661	2,687	291	253	1,190	866	647	919	138	97	1,371	1,311
Delaware-----	928	957	155	118	268	231	251	247	24	40	204	204
Dist. Columbia-----	7,627	6,741	964	765	1,794	1,746	4,539	3,079	119	113	3,777	3,311
Florida-----	25,690	31,815	2,882	3,849	8,319	8,219	11,645	15,714	546	772	14,879	12,511
Georgia-----	14,377	25,698	2,863	3,645	5,713	12,111	5,367	9,255	429	684	8,939	11,011
Idaho-----	585	442	219	160	115	31	199	194	22	20	787	511
Illinois-----	25,723	27,057	3,414	3,052	5,680	5,646	16,083	17,678	546	681	21,014	18,311
Indiana-----	7,945	12,154	1,188	1,580	810	449	2,899	4,673	232	392	3,059	4,411
Iowa-----	2,215	2,588	434	340	569	816	984	1,163	136	94	1,638	1,411
Kansas-----	2,686	3,657	549	702	565	486	1,470	1,858	102	101	1,700	2,311
Kentucky-----	6,204	11,537	977	1,420	1,353	2,534	2,641	4,944	248	364	3,405	3,311
Louisiana-----	16,204	17,158	2,884	2,357	4,280	5,094	4,353	7,680	419	501	13,247	7,611
Maine-----	1,005	946	218	208	140	160	499	421	93	87	1,295	711
Maryland-----	12,559	17,043	1,539	1,204	1,858	1,375	2,795	2,093	119	196	6,164	7,411
Massachusetts-----	5,173	5,079	1,059	937	(§)	(§)	3,793	3,895	319	245	4,626	4,411
Michigan-----	16,012	12,705	2,319	1,743	4,292	2,807	6,827	5,767	411	434	10,412	7,911
Minnesota-----	2,202	2,737	212	221	248	299	1,594	2,048	103	102	1,754	1,311
Mississippi-----	23,905	35,610	8,165	8,928	6,737	11,970	7,953	13,314	1,046	1,398	27,602	30,211
Missouri-----	9,551	8,525	1,657	1,388	2,451	1,678	4,678	4,101	325	223	5,792	4,311
Montana-----	405	450	101	149	60	32	153	214	7	9	275	311
Nebraska-----	1,269	1,855	193	213	527	474	468	1,070	37	63	1,302	1,511
Nevada-----	714	719	62	0	100	121	484	454	24	14	360	211
New Hampshire-----	273	291	42	30	54	24	142	204	20	21	167	111
New Jersey-----	10,091	10,093	1,213	1,208	2,992	2,678	5,459	5,748	391	348	4,773	5,911
New Mexico-----	1,878	2,161	389	372	445	507	958	1,158	76	106	1,323	711
New York-----	32,878	34,389	4,907	3,627	5,936	5,359	20,690	4,296	929	1,160	17,503	14,911
North Carolina-----	10,201	16,093	2,801	3,389	4,083	6,808	3,130	5,524	187	372	8,456	10,311
North Dakota-----	285	301	88	39	52	54	80	136	23	16	239	211
Ohio-----	21,392	21,780	3,449	3,177	5,224	5,066	11,088	12,590	850	947	5,355	4,111
Oklahoma-----	7,392	10,192	1,003	1,489	2,015	3,803	2,700	2,632	276	305	4,976	4,111
Oregon-----	1,889	1,298	568	254	137	114	1,124	846	60	67	2,402	1,211
Pennsylvania-----	12,368	6,825	1,600	1,132	4,453	3,724	4,497	1,238	593	165	(*)	(*)
Rhode Island-----	934	1,023	115	40	99	78	634	786	23	34	823	411
South Carolina-----	14,333	18,678	2,969	3,906	5,571	7,935	5,128	6,132	328	404	5,596	5,511
South Dakota-----	434	484	104	94	84	157	214	179	30	22	333	211
Tennessee-----	17,177	22,138	2,178	2,814	6,954	7,621	7,414	10,934	398	535	12,245	10,011
Texas-----	22,378	42,938	3,094	5,337	6,931	9,344	9,066	14,234	718	1,520	10,391	14,411
Utah-----	743	627	186	201	98	78	444	332	15	12	567	611
Vermont-----	253	245	75	122	80	3	86	108	11	12	185	111
Virginia-----	14,314	16,244	3,815	4,772	5,507	5,895	4,576	4,989	247	362	11,326	7,911
Washington-----	3,773	3,371	750	691	824	523	1,693	1,740	114	111	6,700	5,311
West Virginia-----	3,294	4,992	596	789	517	856	766	1,346	110	163	2,161	2,711
Wisconsin-----	843	1,019	165	197	0	1	670	801	8	21	989	711
Wyoming-----	1,029	596	111	150	167	25	506	239	29	14	169	211
<i>Territories, Possessions, and Panama C. Z.</i>												
Alaska-----	95	140	51	43	15	36	17	34	1	6	420	511
Hawaii-----	908	1,044	189	269	100	121	594	527	60	66	1,657	1,211
Puerto Rico-----	13,216	8,555	1,459	1,817	2,411	1,357	4,451	2,957	1,837	1,496	3,722	2,811
Virgin Islands-----	176	207	27	54	105	114	35	26	8	9	243	111
Canal Zone-----	1,303	(*)	125	(*)	279	(*)	865	(*)	25	(*)	382	(*)
Actual total† of U.S., Territories and Canal Zone-----	441,878	526,202	74,270	79,296	117,797	139,442	194,514	213,276	14,501	16,851	284,410	257,274

\*Data not available.

\*\*Includes "not stated."

†Based on States reporting in both fiscal periods.

‡Includes all reported cases.

§Included in late and late latent.

||Based on 48 States.



# New Cases of Syphilis and Gonorrhea in Cities of 200,000 Population and Over

Health officers' monthly statement: Reported for the first 11 months of the fiscal years 1943-44 and 1942-43

City	Cases of syphilis and gonorrhea reported for first 11 months of fiscal years below											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital		1943-44	1942-43
	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43		
Actual total†	1142,230	1149,304	117,748	116,727	1132,141	1128,492	1163,913	1171,385	112,859	113,004	1172,009	1163,309
Kron	804	1,175	116	165	185	229	442	729	47	52	294	252
Atlanta	2,537	3,834	657	863	772	1,396	1,193	1,541	26	34	1,379	929
Baltimore	9,525	13,325	1,184	906	1,186	945	2,250	1,580	65	74	2,427	3,487
Birmingham	4,430	5,899	280	510	1,157	1,711	1,151	1,530	78	138	532	808
Boston	1,691	1,890	321	292	0	147	1,069	1,211	50	68	1,249	1,099
Buffalo	1,810	1,751	210	143	208	48	1,349	1,497	43	63	829	926
Chicago	15,214	15,576	2,290	2,118	3,422	3,297	9,178	9,776	324	385	12,151	11,879
Cincinnati	2,709	3,395	379	390	(*)	(*)	2,330	(*)	0	0	863	908
Cleveland	4,052	3,720	781	624	1,280	894	1,901	2,074	90	128	1,436	1,284
Columbus	1,454	1,459	313	189	326	302	753	911	42	57	302	348
Dallas	2,352	2,970	465	393	507	537	1,359	2,006	19	32	698	1,012
Dayton	1,553	1,165	173	160	430	220	899	741	51	40	596	238
Denver	1,678	2,124	386	410	464	416	618	1,194	48	51	1,561	1,128
Detroit	11,045	8,508	1,439	1,090	3,523	2,101	5,876	5,129	207	188	5,370	4,690
Honolulu	498	623	63	211	62	79	328	290	44	43	1,045	1,017
Houston	1,849	3,968	341	282	653	1,312	796	2,273	59	101	2,057	1,128
Indianapolis	2,148	3,634	501	582	101	72	511	833	28	31	156	423
Jersey City	430	648	46	53	87	109	286	457	21	29	41	46
Kansas City	1,687	1,831	283	263	305	241	1,014	1,156	70	76	919	872
Los Angeles	10,561	9,613	0	766	4,226	2,681	6,024	5,901	311	265	4,749	4,465
Louisville	1,851	2,226	328	272	340	400	806	1,343	31	53	901	1,109
Memphis	6,757	7,451	548	614	3,140	2,791	2,949	3,827	97	101	4,717	2,788
Milwaukee	468	520	59	72	5	5	388	437	3	6	197	103
Minneapolis	637	772	103	80	117	127	395	547	19	21	679	597
Newark	1,991	2,211	286	304	537	612	1,110	1,243	58	42	804	891
New Orleans	2,192	3,088	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	1,904	1,283
New York	22,936	24,214	4,159	3,284	5,230	4,619	12,685	14,911	584	643	12,645	10,405
Oakland	1,666	1,302	171	150	414	331	1,022	769	39	30	1,329	883
Oklahoma City	1,905	2,092	218	323	489	666	576	687	42	26	1,028	734
Omaha	554	963	61	105	256	209	201	597	27	41	465	604
Philadelphia	8,985	4,489	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	902	(*)
Pittsburgh	(*)	7,955	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	235
Portland	838	667	240	131	50	44	533	460	15	33	1,056	530
Providence	437	481	59	27	44	31	287	384	8	11	149	158
Rochester	259	295	44	44	15	2	193	238	7	11	263	198
St. Louis	5,796	3,959	767	491	1,880	1,181	2,954	2,144	185	18	2,066	1,012
St. Paul	262	471	31	52	38	68	169	321	12	17	255	180
San Antonio	(*)	1,716	(*)	125	(*)	447	(*)	1,071	(*)	57	(*)	932
San Diego	1,042	991	124	93	292	347	541	529	32	21	904	606
San Francisco	2,665	3,139	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	2,014	2,620
Seattle	1,253	1,282	175	164	226	191	773	832	23	22	1,559	1,331
Syracuse	866	862	23	19	26	3	794	821	23	19	311	192
Toronto	843	721	124	92	148	128	540	466	31	34	109	146
Washington, D.C.	7,627	(*)	964	(*)	1,794	(*)	4,539	(*)	119	(*)	3,777	(*)
Actual total†	149,857	158,975	18,712	16,852	33,935	28,939	70,782	72,456	2,978	3,061	76,688	64,476

\*Data not available.

\*\*Includes "not stated."

†Based on cities reporting in both fiscal periods.

‡Includes all reported cases.

1Based on 41 cities.

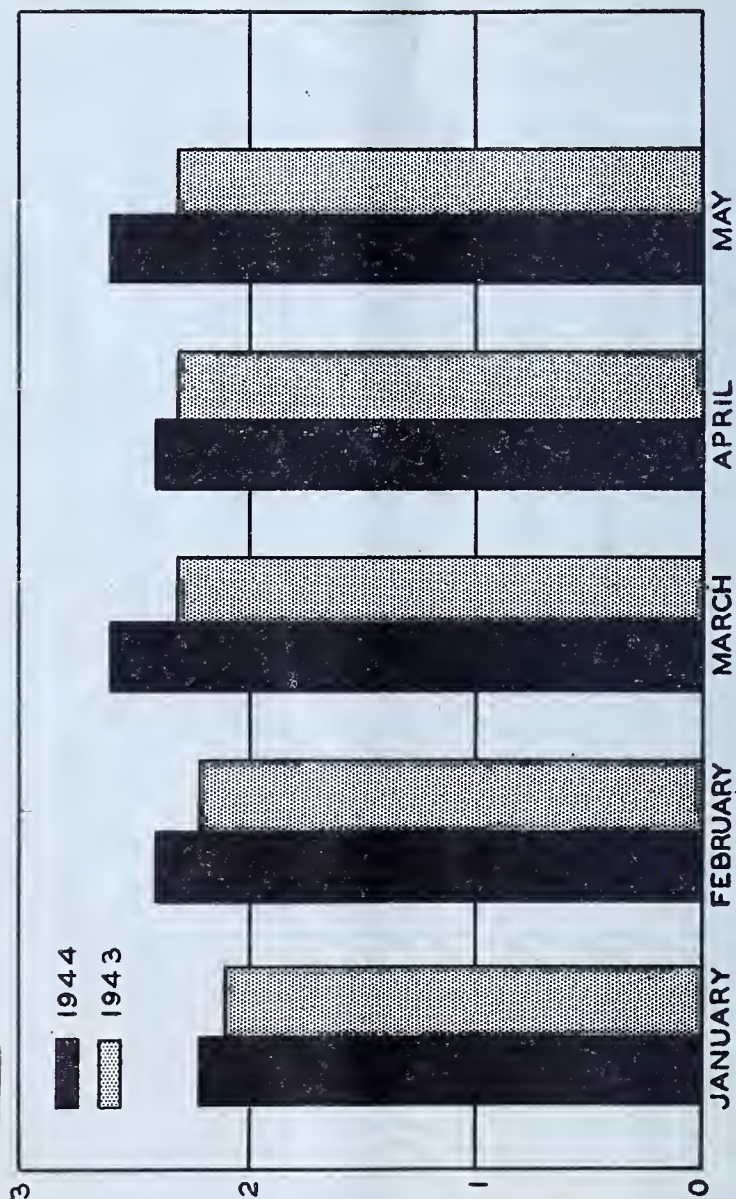
2Based on 38 cities.

3Based on 37 cities.

4Based on 40 cities.

# ANNUAL GONORRHEA CASE RATES IN THE UNITED STATES

## BASED ON PROVISIONAL MONTHLY DATA, 1944 AND 1943



ESTIMATED RATE PER 1,000 POPULATION



# Venereal Disease Information

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FEDERAL SECURITY AGENCY  
UNITED STATES PUBLIC HEALTH SERVICE

THOMAS PARRAN, *Surgeon General*

Editor: J. R. HELLER, Jr., *Medical Director*  
*Chief, Venereal Disease Division*

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# The Treatment of Gonorrheal Urethritis in the Male: Special Reference to the Care of Sulfonamide Resistant Infections with Combined Fever and Sulfathiazole

Eugene Greenwald, Major, Medical Corps, A. U. S.\*

Since the advent of the sulfonamides in the thirties and, more recently, of penicillin, the treatment of gonorrhea has divorced itself from the specialist and has become "legitimately" the realm of the general practitioner. Today the urologist is concerned only rarely in its treatment. Urethral injections, beautifully varicolored and antiseptic urines, prostatic massages and the passage into the urethra of formidable appearing sounds have been transformed to the modest "so many pills" a day.

A series of cases, comprised of 770 enlisted men, was collected and detailed in the past 14 months by the Genito-Urinary Service of the Station Hospital, Fort Belvoir, Va. Seventy-five percent of the men had acute, and 25 percent chronic gonorrheal urethritis. All were treated similarly, being given sulfathiazole in the following dosage: 4 gm. on admission, 2 gm. every 4 hours for five doses, and 1 gm. five times daily for a total of 5 days. No local therapy was used.

Under this rather intensive therapy we have had very few complications referable to treatment (table 1). Although sulfathiazole was used for a 5-day period, no renal complications were encountered in this series. The impression gained from the literature is that there is a low fre-

quency of renal crystallization due to sulfadiazine. Contrary to this, the only sulfonamide kidney complications seen in our genitourinary department have been complete blockages of the ureters coincident with the use of sulfadiazine for other conditions.

Under this intensive regime, 85 percent of the cases were cured with one course, and an additional 7 percent with a second course of sulfathiazole (table 2).

TABLE 2.—Results of treatment

	No. cases	Percent
Cured, 1 course.....	658	85.5
Cured, 2 courses.....	52	6.7
No response.....	60	7.8
Total .....	770	100.0

When it became apparent that sulfonamide resistant infections were to become a mounting problem due to the limited available facilities for mechanical hyperthermia, we initiated "combined" therapy with sulfathiazole and hyperpyrexia induced by intravenous typhoid vaccine. If efficacious, this method would be available to all medical officers without specialized apparatus or training for the treatment of these infections.

The patients in this series were selected solely on the basis of their sulfonamide resistant gonorrhea. Those who were accepted for the course of fever therapy were carefully examined both generally and locally, though no local genitourinary complications precluded its use.

The series was divided into two groups. Group A consisted of soldiers who received an initial dose of 50 million bacilli of typhoid vaccine, with each subsequent dose increased by 50 million at 2-day intervals. Group B was comprised of 32 patients who, following the initial 50 million injection, received a 75 million increment, added to the

TABLE 1.—Complications of treatment

Leukopenia .....	20
Hyperpyrexia .....	7
Gastrointestinal .....	11
Toxicoderma .....	4
Conjunctivitis .....	8
Total .....	50
	or 6.6 percent

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basic dose as a "booster," at each injection. In this latter group it was found possible to attain a higher and more sustained fever reaction (table 3).

During this fever therapy, sulfathiazole was used in the dosage of 1 gm. five times a day for the entire course. On the days of fever induction the fluid intake was maintained at a total of 3,000 cc. per day. Saline by mouth was given to replace the chlorides lost by sweating and occasional emesis. A mild sedative, such as nembutal or bromides, appeared to make the paroxysms more bearable.

All of the patients who were given this combined therapy completed the treatment. About 5 percent of them complained of moderate to severe transient abdominal pain, usually limited to the upper left quadrant. Three percent complained of moderate precordial distress. The most disturbing side action of this treatment was a severe frontal headache, which occurred within an hour after the intravenous injection of the vaccine and subsided only after the temperature had become normal. In a few cases the headache was so severe that the patient submitted to continued therapy with reluctance.

About 95 percent of these patients developed a herpes simplex of the lips, nose or cheek, during or soon after the second paroxysm. Leukopenia was encountered in 10 percent of the patients, but in only 1 case did the count fall below 3,000. These patients were given intramuscular liver extract every other day as a prophylaxis against a continued drop in granulocytes.

The over-all cure-rate of sulfonamide resistant gonorrhea, when subjected to combined sulfathiazole and induced fever as outlined above, was 68 percent. There

seemed to be no significant difference between the two groups, nor did it appear that the special effort made to increase the duration and the height of the induced fever by higher dosage with "booster" injections was of particular added value.

The criterion of cure was complete freedom from gonorrheal infection for 6 months. These men were observed at weekly intervals for 3 weeks, followed by monthly observation for 6 months. Spreads and cultures from the urethra and prostate were obtained on the third week of observation and thereafter when indicated by any residual urethral discharge. Shreds in the first glass or prostatic fluid which had an excess of 10 pus cells per high-power field were viewed with suspicion and checked for gonococci.

It has been our experience that those cases which will not respond either continue with a positive urethral discharge in the face of induction of fever, or relapse within the first 3 weeks of observation. However, to evaluate our results more critically, the reported cases were all observed for 6 months or longer.

COMMENT

Sulfonamide resistant gonorrhea is becoming a mounting problem to the medical profession. There is both an apparent and actual increase in the number of infected patients in whom the disease seems to respond poorly to a treatment routine which, at its inception, appeared to be highly effective. In our personal experience, the problem has become a major cause for anxiety. At this Army post since 1941 the actual incidence of gonorrhea has been decreasing, but the number of sulfonamide resistant infections has trebled.

TABLE 3.—Analysis of combined therapy

Group	Cases	Race		Classification		Complications				Fever induced		Cured	
		White	Negro	Acute	Chronic	Posterior urethritis	Cowperitis	Seminal vesiculitis	Stricture	Average temperature	Average highest temperature	Number	Percent
A.....	23	22	1	14	9	11	2	1	2	101.9°	103.2°	16	69
B.....	82	28	4	27	5	15	1	2	2	103.7°	105.2°	21	67



This increasing chemoresistance of the gonococcus has its counterpart in vitro. Boak and Carpenter reported (1), as early as 1939, that the organism develops some immunity to the drug when exposed to increasing concentrations. This chemoresistant character has proved constant in successive subcultures (2), which conformed to the attested stability of drug-fast strains. The organism usually shows no morphologic changes. Jones (3) found that the changes that had occurred in the presence of sulfonamides were rapidly lost, and that the typical characteristics of the organism were reassumed under suitable cultural conditions.

With the more common and even promiscuous use of sulfonamides, it does not tax the imagination much to picture the increasingly frequent exposure of the gonococcus at large to sulfonamides. As the organism has been subjected more frequently to this sulfonamide environment, an increasing number of strains have apparently developed chemoresistance. Further favoring this new bacterial characteristic, many patients are receiving suboptimal dosage, especially when either self or drug store treated. That this fact is a major cause for the evolution of resistant strains is a distinct possibility, though many patients with apparently adequate dosage fail to conquer the disease. Gold (4) has shown that various organisms, including the gonococcus, are able to acquire drug-fastness if exposed to sublethal dosage, and that this may develop most rapidly within 3 days.

Probably immunologic factors involved in the host explain the lack of response. What these are one can only speculate. They may include the general physical condition, the status of general immunity response and, apparently, the race of the patient. It has been our experience that sulfonamide resistant infections are comparatively rare in the Negro, being 20 times more common in the white soldier at this station. Whether this unusual preponderance depends upon the strain of the infecting organism in the Negro subject or upon the difference in the basic immunology of the two races is an interesting question to settle.

This problem was considered by Schnetz

(5) who believes that during chemotherapy there is a biphasic action: inhibition of bacterial growth by the sulfonamide and destruction of the damaged organisms by phagocytosis and bacteriolysis. This conception must also include a second factor, immunobiologic, to account for those cases of fresh infection which respond poorly to what is adequate therapy for the average. Investigation of this "host" factor in "host" serum reveals that the bacteriocidal properties consist of two components which are nonspecific and differ individually. Cases of gonorrheal infection in which chemotherapy fails often show a high serum resistance.

This serum resistance, as has been shown by Landy and Dicken (6), depends almost in toto on the ability of the organism to manufacture para-aminobenzoic acid. They have shown that the sulfonamide resistance of a strain of gonococcus can be foretold mathematically by PAB titrations, i. e., the higher the PAB production the more likely that the organism will not respond to sulfonamide therapy.

Fever therapy has been used successfully by Trautman (7), Ferguson and coworkers (8), and others (9, 10). All the investigators are agreed on the excellent results of mechanical hyperthermia. Ferguson and coworkers (11) used essentially the method of fever induction with typhoid vaccine to which our group A cases were subjected. He did not use sulfathiazole coordinately with the fever and his results showed that approximately 5 percent were cured with fever alone; 64 percent were cured with fever followed by another course of sulfathiazole. It is interesting to speculate upon what effect the fever or what nonspecific effect the typhoid vaccine had upon the organism to change its essential character from sulfonamide resistance to sulfonamide sensitivity. Another possibility must be considered, that is, a potentiation of the immunologic response of the host following the induction of fever, increasing his destructive efficiency.

Our series was separated into the two groups in order that we might determine, to some rough degree, whether the therapy was essentially a nonspecific effect upon the

immunology of the host, or a change in the sensitivity of the organism during the fever induction. We could not consider that the high temperatures attained in group B were lethal, since they only approximate the thermal death point of the gonococcus. By referring to table 3, it can be seen that there is essentially no difference in the results of the two groups. The total effect is apparently nonspecific, and attaining a higher and more prolonged fever by the method of booster injections is not justified.

In the discussion of sulfonamide resistant infections, penicillin must be considered as the drug of choice. The cases that have been reported, though very few, have shown excellent results. Though the use of penicillin must be considered as experimental, a General Hospital, which is completing a penicillin-treated series of sulfonamide resistant gonorrheal infections, reports almost universal cure. Perhaps, as the strains of gonococci are more frequently exposed to penicillin, we may expect in the future to find penicillin-fast strains. With the present rapid chemotherapeutic strides, still another lethal weapon may be developed to replace those that have become ineffective.

#### SUMMARY

1. When administered in the dosage recommended sulfathiazole therapy was effective in 85 percent of unselected cases of gonorrheal urethritis in the male.
2. An additional 7 percent were cured by a second course of treatment.
3. When the sulfathiazole routine, as outlined, was limited to 5 days for the average gonorrheal urethritis, complications occurred in 6.6 percent, but only rarely did they indicate cessation of treatment.
4. Sulfonamide resistant gonorrhea is encountered more frequently in the white man than the Negro.
5. Pyrexia induced by intravenous typhoid vaccine in conjunction with sulfathia-

zole cured 68 percent of routine treatment failures.

6. The complications following combined fever and sulfathiazole therapy were never severe enough to justify termination of therapy.

7. If a relapse is to occur, it usually does so within the first month of observation.

8. The combined therapy advocated is another weapon in the hands of the physician who has no access to mechanical hyperthermia or to penicillin.

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# Venereal Disease Epidemiology in the Army Third Service Command: Progress Report for Period July Through December 1943

E. W. Norris, Senior Surgeon, U.S.P.H.S.<sup>1</sup>, A. F. Doyle, Major, M.C.<sup>2</sup>, Fred W. Kratz, Senior Surgeon, U.S.P.H.S.<sup>3</sup>, and Albert P. Iskrant, M.A., U.S.P.H.S.<sup>4</sup>

In December 1942 (1) and June 1943 (2) we presented data regarding 10,540 contacts reported by soldiers in camps in the Third Service Command. These tabulations, as well as those for the period July through December 1943, were prepared with the aid of the U. S. Public Health Service Central Tabulating Unit. The three series of data are presented here so that comparative figures may be available and any trends determined in the type of information reported by soldiers or the type of individual to whom the soldier is exposed.

Of the 5,906 contacts reported in this 6-month period, 60 percent (3,557) occurred within the geographical boundaries of the Third Service Command (Maryland, Pennsylvania and Virginia) and 40 percent (2,349) outside. Soldiers in camps in the Third Service Command reporting with venereal disease during this period were exposed to persons living in every State in the United States.

In table 1 an improvement is apparent in the number of reports containing information considered adequate for location of the contact. This improvement was shown for both white and Negro. That the improvement in the type of information is real is indicated by the fact that there was a slight increase in the percentage located of cases so classified.

The only significant change in the type of contact, place of encounter or place of exposure, except what could be accounted for by seasonal trend, is a continuous decline in the percentage of contacts which may be considered paid prostitutes and a

decrease in the percentage (and number) of exposures in brothels. The brothel is obviously on the way out, and it is not being accomplished by an increase in the number of other types of prostitute. It should be pointed out that the term "contact" includes "spread" as well as "source" contacts; therefore, as is to be expected with the increased drafting of married men, the proportion of contacts described as "wife" has increased.

Previous tabulations presented data on the results of investigations allowing at least 60 days for the closing of an investigation. No significant change was noted in the tabulation prepared for the current period. As many investigations are closed after the expiration of the 60-day period, we have prepared a tabulation (table 6) showing the disposition as of Dec. 31, 1943 of the cases reported in the period January through June 1943. At least 6 months, therefore, has been allowed to close the investigations.

Two-thirds of all the reports of contacts referred by camps and stations in the Third Service Command to health authorities were returned with a result of investigation checked. The case was located in approximately one out of every four contacts reported. When only forms on which apparently adequate information is given are considered, results of investigation were returned in 76 percent and the case located in one out of every two cases (55 percent).

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TABLE 1.—Completeness of information—Army contacts, Third Service Command  
(Comparison between periods March–December 1942, January–June 1943 and July–December 1943)

Race	Period	Sufficient information for possible location of the contact		Sufficient information for referral for possible location of foci of infection		Insufficient information for referral for any purpose		Total contacts reported	
		Number	Percent	Number	Percent	Number	Percent	Number	Percent
White	Mar.–Dec. 1942---	462	24.3	557	29.4	878	46.3	1,897	100.0
	Jan.–June 1943---	712	27.7	946	36.8	914	35.5	2,572	100.0
	July–Dec. 1943---	946	39.6	573	24.0	870	36.4	2,389	100.0
Negro	Mar.–Dec. 1942---	871	33.0	672	25.5	1,096	41.5	2,639	100.0
	Jan.–June 1943---	1,062	32.0	1,057	31.9	1,198	36.1	3,317	100.0
	July–Dec. 1943---	1,461	41.7	781	22.3	1,258	35.9	3,500	100.0
Total*	Mar.–Dec. 1942---	1,358	29.3	1,261	27.2	2,022	43.5	4,641	100.0
	Jan.–June 1943---	1,775	30.1	2,007	34.0	2,117	35.9	5,899	100.0
	July–Dec. 1943---	2,412	40.8	1,356	23.0	2,138	36.2	5,906	100.0

\* Total includes race "other or unknown."

TABLE 2.—Type of contact—Army contacts, Third Service Command  
(Comparison between periods March–December 1942, January–June 1943 and July–December 1943)

Race	Period	Wife		Friend		Pick-up, no fee		Street-walker		Brothel		Call girl		Other		Total known		Total contacts
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	
White	Mar.–Dec. 1942...	109	6.3	248	14.4	1,107	64.1	133	7.7	106	6.1	21	1.2	3	0.2	1,727	100.0	1,897
	Jan.–June 1943...	268	10.5	558	21.8	1,431	56.0	150	5.9	80	3.1	53	2.1	15	0.6	2,555	100.0	2,572
	July–Dec. 1943...	472	19.9	503	21.3	1,237	52.3	102	4.3	37	1.6	15	0.6	2	0.1	2,368	100.0	2,389
Negro	Mar.–Dec. 1942...	161	6.8	528	22.3	1,063	44.9	454	19.2	149	6.3	6	0.2	7	0.3	2,368	100.0	2,639
	Jan.–June 1943...	265	8.0	1,059	32.1	1,255	38.0	612	18.5	101	3.1	6	0.2	2	0.1	3,300	100.0	3,317
	July–Dec. 1943...	587	16.9	1,054	30.3	1,301	37.4	483	13.9	53	1.5	2	0.1	—	—	3,480	100.0	3,500
Total*	Mar.–Dec. 1942...	276	6.6	784	18.7	2,237	53.4	596	14.2	262	6.3	27	0.6	10	0.2	4,192	100.0	4,641
	Jan.–June 1943...	535	9.1	1,618	27.6	2,690	45.9	762	13.0	183	3.1	60	1.0	17	0.2	5,865	100.0	5,899
	July–Dec. 1943...	1,060	18.1	1,561	26.6	2,543	43.4	586	10.0	93	1.6	17	0.3	2	—	5,862	100.0	5,906

\* Total includes race "other or unknown."

TABLE 3.—Age of nonfamilial contacts—Army contacts, Third Service Command  
(Comparison between periods January–June 1943 and July–December 1943)

Type of contact and race	Period	10–14		15–19		20–24		25–29		30–34		35–44		45 and over		Total known		Total contacts
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	
Clandestine White	Jan.–June 1943	1	0.1	491	25.0	960	48.9	361	18.3	113	5.8	36	1.8	1	0.1	1,963	100.0	1,989
	July–Dec. 1943	1	0.1	407	23.7	841	49.1	329	19.2	90	5.3	42	2.5	5	0.3	1,714	100.0	1,740
Negro	Jan.–June 1943	—	—	944	41.5	1,000	44.0	252	11.1	60	2.6	15	0.7	1	0.1	2,272	100.0	2,314
	July–Dec. 1943	6	0.3	924	39.9	1,045	45.1	260	11.2	60	2.6	21	0.9	1	0.1	2,317	100.0	2,355
Paid prostitute White	Jan.–June 1943	—	—	32	11.6	128	46.4	95	34.4	15	5.4	5	1.8	1	0.4	276	100.0	283
	July–Dec. 1943	—	—	23	15.1	66	43.4	43	28.3	13	8.6	7	4.6	—	—	152	100.0	155
Negro	Jan.–June 1943	—	—	154	22.1	373	53.4	132	18.9	34	4.9	5	0.7	—	—	698	100.0	719
	July–Dec. 1943	—	—	129	24.6	285	54.4	84	16.0	22	4.2	4	0.8	—	—	524	100.0	538
Total nonfamilial*	Jan.–June 1943	1	—	1,622	31.1	2,466	47.3	842	16.1	222	4.2	61	1.2	3	0.1	5,217	100.0	5,313
	July–Dec. 1943	7	0.1	1,486	31.5	2,241	47.5	716	15.2	185	3.9	74	1.6	6	0.2	4,715	100.0	4,801

\* Total includes race "other or unknown."



TABLE 4.—Place of procurement or encounter—nonfamilial contacts, Third Service Command  
(Comparison between periods March–December 1942, January–June 1943 and July–December 1943)

Type of contact and race	Period	Bus or rail-road depot		Hotel		Cab		Street		Tavern <sup>1</sup>		Dance hall		Home or apartment		Other		Total known		Total contacts
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	
Clandestine White	Mar.–Dec. 1942	45	3.6	30	2.4	6	0.5	405	32.2	504	40.1	47	3.7	79	6.3	141	11.2	1,257	100.0	1,355
	Jan.–June 1943	82	4.3	52	2.7	3	0.2	359	18.9	909	47.9	75	4.0	229	12.0	189	10.0	1,898	100.0	1,989
	July–Dec. 1943	64	3.9	39	2.4	1	—	412	25.1	671	40.8	60	3.7	218	13.3	178	10.8	1,643	100.0	1,740
Negro	Mar.–Dec. 1942	17	1.2	19	1.4	2	0.1	405	28.7	465	33.0	48	3.4	256	18.2	197	14.0	1,409	100.0	1,591
	Jan.–June 1943	36	1.7	12	0.6	1	—	345	15.8	722	33.1	126	5.7	702	32.2	237	10.9	2,181	100.0	2,314
	July–Dec. 1943	40	1.8	25	1.1	—	—	430	19.4	674	30.3	105	4.7	724	32.6	223	10.1	2,221	100.0	2,355
Paid prostitute White	Mar.–Dec. 1942	3	1.2	38	15.5	3	1.2	58	23.7	56	22.9	2	0.8	2	0.8	83	33.9	245	100.0	260
	Jan.–June 1943	5	1.9	60	22.1	8	3.0	65	24.0	64	23.6	2	0.7	10	3.7	57	21.0	271	100.0	283
	July–Dec. 1943	3	2.0	27	18.1	2	1.3	40	26.8	37	24.8	—	—	6	4.0	34	22.8	149	100.0	155
Negro	Mar.–Dec. 1942	7	1.2	10	1.7	—	—	208	35.3	212	36.0	16	2.7	27	4.6	109	18.5	589	100.0	609
	Jan.–June 1943	12	1.7	8	1.1	1	0.2	214	30.4	290	41.1	26	3.7	41	5.8	113	16.0	705	100.0	719
	July–Dec. 1943	11	2.1	5	1.0	—	—	202	38.8	187	35.9	15	2.9	38	7.3	63	12.1	521	100.0	538
Total nonfamilial <sup>2</sup>	Mar.–Dec. 1942	74	2.1	97	2.7	11	0.3	1,099	30.7	1,271	35.5	113	3.2	364	10.2	546	15.3	3,575	100.0	3,906
	Jan.–June 1943	135	2.7	133	2.6	13	0.3	985	19.5	1,987	39.2	230	4.5	982	19.4	598	11.8	5,063	100.0	5,313
	July–Dec. 1943	118	2.6	96	2.1	4	0.1	1,090	24.0	1,569	34.5	181	4.0	988	21.7	500	11.0	4,546	100.0	4,801

<sup>1</sup> Includes cafe, restaurant, night club.  
<sup>2</sup> Total includes race "other or unknown."

TABLE 5.—Place of exposure—nonfamilial contacts, Third Service Command  
(Comparison between periods March–December 1942, January–June 1943 and July–December 1943)

Type of contact and race	Period	Home or apartment		Hotel or rooming house		Cab		Auto or trailer		Brothel		Outdoors		Tourist cabin		Other		Total known		Total contacts
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	
Clandestine White	Mar.–Dec. 1942	252	19.4	302	23.3	23	1.8	411	31.7	—	—	177	13.7	82	6.3	49	3.8	1,296	100.0	1,355
	Jan.–June 1943	459	23.5	591	30.3	31	1.6	495	25.4	—	—	186	9.5	141	7.2	48	2.5	1,951	100.0	1,989
	July–Dec. 1943	368	21.5	400	23.4	20	1.2	480	28.1	—	—	324	18.9	82	4.8	36	2.1	1,710	100.0	1,740
Negro	Mar.–Dec. 1942	686	46.4	299	20.2	8	0.5	293	19.8	—	—	108	7.3	9	0.6	77	5.2	1,450	100.0	1,591
	Jan.–June 1943	1,115	49.8	569	25.4	9	0.4	354	15.8	—	—	129	5.8	5	0.2	58	2.6	2,239	100.0	2,314
	July–Dec. 1943	1,134	48.7	481	20.7	13	0.6	426	18.3	—	—	224	9.6	3	0.1	47	2.0	2,328	100.0	2,355
Paid prostitute White	Mar.–Dec. 1942	16	6.2	77	30.0	13	5.1	16	6.2	105	40.9	14	5.4	8	3.1	8	3.1	257	100.0	260
	Jan.–June 1943	28	10.1	106	38.1	15	5.4	18	6.4	79	28.4	13	4.7	11	4.0	8	2.9	278	100.0	283
	July–Dec. 1943	17	11.0	64	41.6	3	1.9	18	11.7	39	25.3	2	1.3	8	5.2	3	1.9	154	100.0	155
Negro	Mar.–Dec. 1942	169	29.1	131	22.5	2	0.3	37	6.4	185	31.8	24	4.1	2	0.3	32	5.5	582	100.0	609
	Jan.–June 1943	205	29.9	243	35.5	6	0.9	29	4.2	145	21.2	26	3.8	1	0.1	30	4.4	685	100.0	719
	July–Dec. 1943	193	36.5	191	36.1	—	—	28	5.3	59	11.2	25	4.7	2	0.4	31	5.9	529	100.0	538
Total nonfamilial*	Mar.–Dec. 1942	1,135	30.7	827	22.4	47	1.3	773	20.9	297	8.0	342	9.3	104	2.8	171	4.6	3,696	100.0	3,906
	Jan.–June 1943	1,810	35.1	1,511	29.3	61	1.2	896	17.3	225	4.3	355	6.9	158	3.1	144	2.8	5,160	100.0	5,313
	July–Dec. 1943	1,713	36.2	1,138	24.1	37	0.8	954	20.2	100	2.1	576	12.2	95	2.0	118	2.5	4,731	100.0	4,801

\* Total includes race "other or unknown."

TABLE 6—Results of investigation by completeness of information and time of closing of investigation—Army contacts, Third Service Command (January–June 1943)

Apparent completeness of information	Disease	Investigations completed	Not infected		Under treatment as a result of investigation		Under treatment prior to investigation		Total located		Not examined		Insufficient information for investigation		No disposition returned		Total	
			No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Sufficient for location of contact	Syphilis	within 60 days by 12-31-43	71	14.8	64	13.3	34	7.1	169	35.2	37	7.7	1	0.2	274	57.0	481	100.0
	Gonorrhea	within 60 days by 12-31-43	118	24.5	100	20.8	47	9.8	265	55.1	78	16.2	3	0.6	135	28.1	481	100.0
Sufficient for location of foci of infection	Syphilis	within 60 days by 12-31-43	213	15.2	245	17.4	48	3.4	506	36.0	189	12.9	4	0.3	714	50.8	1,405	100.0
	Gonorrhea	within 60 days by 12-31-43	344	24.4	356	25.3	67	4.8	767	54.5	313	22.3	7	0.5	318	22.6	1,405	100.0
Insufficient for any practical purpose	Syphilis	within 60 days by 12-31-43	22	6.1	18	5.0	15	4.1	55	15.2	78	21.5	14	3.9	216	59.5	363	100.0
	Gonorrhea	within 60 days by 12-31-43	33	9.1	25	6.9	24	6.6	82	22.6	109	30.0	15	4.1	157	43.3	363	100.0
Total cases reported*	Syphilis	within 60 days by 12-31-43	106	6.3	138	8.3	30	1.8	274	16.4	370	22.1	98	5.8	938	55.8	1,680	100.0
	Gonorrhea	within 60 days by 12-31-43	172	10.2	204	12.2	44	2.6	420	25.0	560	33.3	127	7.6	572	34.0	1,680	100.0
	Syphilis	within 60 days by 12-31-43	6	1.7	4	1.1	6	1.7	16	4.5	78	21.9	75	21.1	187	52.2	356	100.0
	Gonorrhea	within 60 days by 12-31-43	6	1.7	4	1.1	8	2.2	18	5.0	97	28.3	87	24.4	154	43.2	356	100.0
	Syphilis	within 60 days by 12-31-43	17	1.0	46	2.6	16	0.9	79	4.5	387	21.9	461	26.1	841	47.6	1,768	100.0
	Gonorrhea	within 60 days by 12-31-43	32	1.8	57	3.2	30	1.7	119	6.7	509	28.9	512	30.0	628	35.5	1,768	100.0
	Syphilis	within 60 days by 12-31-43	462	7.2	522	8.1	151	2.4	1,135	17.7	1,198	18.6	689	10.7	3,397	52.9	6,419	100.0
	Gonorrhea	within 60 days by 12-31-43	748	11.7	766	11.9	225	3.5	1,739	27.1	1,762	27.4	798	12.4	2,120	33.0	6,419	100.0

\* Includes 366 cases of "Other V.D."

## DIAGNOSIS

**Gonococcal fixation test.** Correspondence. Brit. J. Ven. Dis., London, 20: 81-82, June 1944.

Price, in a communication to the editor, comments on an article by Harkness on "Drug resistance in gonorrhea," in which it is stated that a positive gonococcic complement fixation test is useless as a test of cure. Price asks concrete evidence in support of this statement.

Harkness, in his reply, states that in view of his vast amount of experience if he were to discard any one test used in any stage of gonorrhea, he would discard the complement fixation test without hesitation. This test, depending as it does on circulating antibodies, has become even more meaningless since the use of sulfonamide therapy. An adequate dosage of chemotherapy taken early in the disease usually cures the infection before the blood becomes positive,

consequently the blood remains negative throughout the period of observation. In cases in which treatment is delayed for a week or longer it often becomes positive and the longer the delay the more likely is it to remain positive after a cure has been effected. The clinician's only difficulties are in the small percentage of failures which are invariably occasioned by drug resistance, associated very rarely with closed foci of infection. Harkness has always had negative results when the resistance is partial and often when the resistance is complete. In cases of complete resistance a positive reaction occurs more frequently after nonspecific protein therapy which may stimulate the formation of large amounts of specific antibodies. One of the chief reasons that Harkness considers a positive reaction as useless as a test of cure is that gonococcic antibodies may persist for months, even throughout life, without any infective focus. He cites instances to substantiate this theory.

Harkness is of the opinion that in view of the frequency of persistent positive reac-



ions which have no clinical significance, physicians and surgeons should not rely upon the gonococcic complement fixation test in the diagnosis of suspected gonococ-  
cic complications.

**A method using solid medium in a delayed gonococcal culture procedure.**

John D. Porterfield and Everett A. Nelson. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, **28**: 417-421, July 1944.

A technic is outlined for the use of a solid medium slant which permits the delayed (6 to 8 hours) culture of gonococci with results significantly better than those obtained by microscopic examination of spreads. Routine cultures made on 151 specimens at the Wayne County venereal disease clinics resulted in 20 (13.3 percent) positive findings which would have been missed by spread alone.

With a lapse of 6 to 8 hours between inoculation and incubation it is possible for physicians and small clinics to transport inoculated tubes to a central laboratory where gonococcic culture is done routinely. The solid medium facilitates transportation and minimizes chances of accident to the inoculum between inoculation and incubation. It has also the considerable advantage of eliminating transfer of inoculum since the original inoculation is made directly on the culture medium.

The method with a 24-hour delay is not as efficient in its present form as the plate. If further study or improvement of the method produces adequate results after a 24-hour delay before incubation, the method will permit the development of a mailing service.

**Primary syphilis of the rectum and gonorrhea of the anus in a male homosexual playing the role of a female prostitute.** A. J. Jones and Lee Janis. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, **28**: 453-457, July 1944.

A case is reported of a rectal chancre existing simultaneously with gonorrheal proctitis in a male homosexual who played the role of a female and practiced prostitution as a profession.

One case each of acute gonorrheal urethritis and primary syphilis of the penis were directly traceable to this source.

Both men infected by the patient believed that they had had sexual intercourse with a woman per vaginam, and emphatically denied even a suspicion of his true sex.

**A case of primary chancre of the bulbar conjunctiva.** C. Dee Shapland. *Brit. J. Ophth.*, London, **28**: 187-189, Apr. 1944.

The patient, a 20-year-old man in the R. M. Division, was admitted to the Ophthalmic Department on May 12, 1943, complaining of inflammation of and slight discharge from the left eye of 10 days' duration. There was slight edema of both lids of the left eye, the plica semilunaris and caruncle of which were prominent in the area exposed in the palpebral fissure which was somewhat narrowed by the edema. The left preauricular and submaxillary lymph nodes were enlarged, firm and discrete. An indurated band of cartilaginous consistency was palpable through the lower lid and easily seen when the lid was everted. The band was directly continuous with the lower end of the enlarged and edematous plica, and laterally became lost on the bulbar conjunctiva infero-temporally. On it at the junction of its inner and middle thirds was a small, grayish-white ulcer, 4 mm. long by 1½ mm. broad, with well-defined sharp edges and gray sloughing base. The bulbar conjunctiva was slightly chemotic and showed a cyanotic tinge. Discharge was very slight. The cornea was bright and showed no stain with fluorescein; the media of the eye were clear and fundus normal.

The diagnosis of primary chancre of the conjunctiva was confirmed by darkfield examination. The blood Wassermann and Kahn reactions were positive.

Treatment, consisting of 0.04 gm. mapharside (mapharsen) intravenously and bismostab 0.2 gm. intramuscularly, was instituted 2 days following admission. This was followed by 0.06 gm. mapharside twice weekly and bismostab injections once weekly until July 2. A total of 0.88 gm. mapharside and 1.9 gm. bismostab was given.

The patient was then transferred to North Wales.

Discharge from the left eye ceased by the third day after the first injection, and the ulcer had completely disappeared by the seventh day. The indurated band in the lower fornix remained unchanged for 2 weeks, but at the end of a month was no longer palpable through the lower lid. Enlargement of the preauricular lymph node had disappeared 2 weeks after the first injection and that of the submaxillary group a week later; however, these lymph nodes remained palpable up to the time of his discharge from the hospital. The left eye had returned to normal except for a somewhat thickened plica at the lower extremity of which the remains of the indurated band curving into the lower fornix was still just visible.

**Biologic false positive spinal fluid Wassermann reactions associated with meningitis: Report of eight cases.** Virgil Scott, Frank W. Reynolds and Charles F. Mohr. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, 28: 431-442, July 1944.

The authors report 7 cases of biologic false positive spinal fluid Wassermann reactions in seronegative nonsyphilitic persons during the course of meningitis, and 1 case in which transfer of reagin from blood to spinal fluid may have occurred. In 3 instances the meningitis was tuberculous, in 2 meningococcal, and in 2 aseptic lymphocytic. The findings in these cases are reported in detail.

The authors conclude that false positive spinal fluid Wassermann tests may occur in syphilitic and nonsyphilitic patients during the course of pyogenic, aseptic and tuberculous meningitis, and perhaps in other types of intracranial disease.

The diagnosis of neurosyphilis based on a positive spinal fluid Wassermann reaction alone is unjustified in patients suffering from meningitis and other acute intracranial disorders until repeated examinations, performed after these processes have subsided, demonstrate the continued presence of reagin.

**Peripheral vascular syphilis of the lower extremities.** Franklin H. Grauer and Harvey L. Myers. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, 28: 458-464, July 1944.

A 23-year-old white soldier was admitted to Stark General Hospital. Examination upon admission disclosed 2 dime-sized, roughly circular, deep-scated, necrotic, punched-out ulcers, involving the medial surface of the left fourth toe and left heel. Their bases were covered with purulent exudate due to secondary pyogenic infection and there was a lymphangitis manifested by reddish streaks along the anteromedial aspect of the lower left leg. The left femoral and inguinal lymph nodes were enlarged and tender. The pulses of both the right and left dorsalis pedis and anterior tibial arteries could not be felt. The pulses of the peroneal and posterior tibial arteries were full and bounding. There was low-grade fever. This condition started 4 months prior to admission.

The patient gave a history of a similar lesion on the right fourth toe 6 months previously. At that time he consulted a civilian physician who amputated the toe at the metatarsophalangeal joint.

The Wassermann and Kahn serologic tests for syphilis were positive.

Further examination failed to disclose any evidence to suggest cardiovascular, hepatic or neuraxial involvement.

A therapeutic test consisting of 0.06 gm. mapharsen twice a week and 0.2 gm. bismuth subsalicylate in oil once a week resulted in complete healing of the lesions after 10 to 14 days. Antisyphilitic treatment was continued and after 16 injections of 0.06 gm. mapharsen and 5 of 0.2 gm. bismuth subsalicylate in oil, physical examination was completely negative except for absent pulsations of the right and left anterior tibial and dorsalis pedis arteries.

The authors report this case because of the scarcity of recorded examples of clinical syphilitic arteritis of the extremities and because a routine preoperative serologic test for syphilis in this instance might have avoided surgical intervention. In cases of peripheral vascular disease with a positive



routine serologic test for syphilis a therapeutic test should first be instituted.

### **Extensive tertiary syphilitic ulceration.**

Clinical records. *Brit. J. Ven. Dis.*, London, 20: 42-44, Mar. 1944.

Although there is no doubt that extensive tertiary syphilitic lesions have become rare, it is evident from the 2 cases cited that they still occur. A 42-year-old laborer, undernourished and in poor physical condition, had acquired a penile sore at the age of 20 for which he was given 1 injection into the buttock. The sore healed in 2 weeks and no further treatment was received. Three years later ulcers appeared over the forehead; these healed months later following local medication. Eighteen years later extensive ulceration appeared around the mouth and nasal orifices; these persisted for 2 years. As they resisted local medication, the patient presented himself to a physician. Examination showed marked scarring with destruction and distortion of the tissues and some areas of active ulceration around the lips and nasal orifices; the nasal septum was largely destroyed and ulceration could be seen within the nasal cavities. The skin of the forehead was widely scarred and adherent to the frontal bones. The skin of the right leg from ankle to hip was a network of "tissue-paper" scars. The Wassermann and Kahn tests were strongly positive. The ulceration responded to 2 injections of a bismuth compound and a moderate dosage of potassium iodide. Four treatments in all were given. The patient was reported dead a few months later.

The second case was a 48-year-old woman, whose only suggestive history of syphilis was a sore throat over a long period at the age of 28. Ulceration of the scalp and face began 12 years later and continued for 1 year when antisypilitic treatment was instituted and continued for some months. Examination of the patient following a 6-year period without treatment revealed destruction of a large area of the scalp which had been replaced by thin scar tissue studded with small oozing sores and adherent to the underlying cranium. X-ray examination showed that the frontal

and parietal bones were widely affected with periostitis of the outer table. There was scattered scarring of the face, contraction of which had produced permanent ectropion of the left eyelid. The internal structures of the nose appeared to have been destroyed. Except for a few small areas on the scalp, there was no active ulceration. The Wassermann reaction had been positive in 1929, but was negative at the time of examination; the Kahn test was positive.

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## **TREATMENT**

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**Herpes following fever therapy.** Richard L. Sutton, Jr. *Bull. U. S. Army M. Dept., Carlisle Barracks, No. 78:* 115-116, July 1944.

Patients with chemoresistant gonorrheal infection treated by mechanically induced fever, 106° F. rectally, maintained for 7 hours, which has been preceded by the administration of 8.0 gm. sulfathiazole over an 18-hour period, have been seen to develop herpes within the next few days following treatment.

Of the 60 patients who received fever therapy, 43 developed herpes. Investigation of their past history showed that 20 had had one or more attacks of herpes a year for several years, 12 had had attacks once or twice in their lifetime, and 11 had never had an attack. In 10 patients who received a second course of therapy, 6 developed herpes after the first fever treatment and 1 after the second. One patient who was given fever treatment three times developed severe herpes after the first treatment, none after the second given 11 days later, and a moderate attack after the third given 13 days after the second. He had had repeated attacks in the past.

Of the 17 patients in whom no herpes appeared after fever therapy, 13 had never had an attack of herpes, 3 had had attacks once or twice, and 1 had had one or more attacks a year for several years.

Of the 21 patients who had had herpes repeatedly, 14 developed moderate or severe

attacks of herpes following fever therapy; of the 39 patients who never had herpes or had had it only once or twice, 15 developed moderate or severe attacks.

From this study the author concluded that individuals with recurrent herpes appeared to suffer more severe postpyrexial herpes than individuals who had never, or only rarely, had herpes. Patients who developed herpes after their first fever treatment seldom had repeated attacks after a second course given within 2 weeks.

**The electrocardiographic changes following artificial hyperpyrexia.** A. Henry Clagett. *Am. J. M. Sc.*, Philadelphia, 208: 81-95, July 1944.

The author describes and explains the electrocardiographic (EKG) changes following artificial hyperpyrexia found in a series of 86 patients who received a total of 118 sessions of fever (80 therapeutic and 38 conditioning fevers).

Of the 80 EKG's following therapeutic fever, 64 showed insignificant changes, 7 showed significant changes, and 9 showed no change whatever from the prefever tracings. Of the tracings taken following conditioning fever, 21 showed no change and 16 showed insignificant changes.

In the administration of therapeutic fevers, an attempt was made to maintain the patient at between 105° and 107° F. for 5 to 10 hours. For the conditioning fever, a body temperature of 101° F. was maintained for 30 minutes. Electrocardiograms were taken routinely on all patients before and after fever therapy, and following conditioning fevers.

The findings in 9 cases are described; 7 showed significant changes, 1 insignificant changes in his postfever tracing but developed significant changes on the following day, and 1 not previously listed. These findings are tabulated.

In the discussion the author points out that of the 9 cases described, 3 had myocardial damage, probably on the basis of small coronary artery occlusions. Two of these cases suffered a relapse 39 and 56 days, respectively, following fever. The remaining 6 showed transient and significant EKG changes following fever, pos-

sibly due to myocardial anoxia rather than myocardial damage.

The author concludes that while the majority of EKG changes following fever therapy are insignificant and probably due to the effect of tachycardia, it is possible to have changes due to severe myocardial damage, such as that caused by occlusion of a small coronary artery. Treatment of these cases should be the same as that given myocardial infarction due to any other cause.

**A suggestion for the production of therapeutic fever in general paresis.** Louis H. Cohen and Virginia Hale. *Yale J. Biol. & Med.*, New Haven, 16: 619-626, July 1944.

The authors believe that the continuous intravenous drip technic with typhoid vaccine, which Knight, Emory and Flint have employed for inducing therapeutic fever in cases of resistant gonorrhea, can be used in the treatment of general paresis. This method is discussed at length. (See also *Venereal Disease Information*, 24: 323-329, November 1943.)

A case in which this treatment was used is described in detail. The patient had completed 10 treatments and had shown gratifying response. When the series was begun, he was markedly confused, dull, asocial, untidy; he also had frequent outbursts of irritability, and prolonged convulsive seizures. After the third treatment he began to show definite improvement. Tryparsamide was given once weekly at the height of the induced fever. The serologic picture has remained unchanged except for the spinal fluid protein which has become somewhat reduced.

The therapeutic efficacy of this treatment cannot be evaluated until a large number of patients have been studied. However, the authors believe that it has the particular advantage over other methods of more effective regulation and control. It also appears to be therapeutically effective in producing fever in the paretic who has become malaria-resistant. (The authors do not state how many patients they have treated by this method.)



**Malarial treatment in the earlier stages of neurosyphilis.** F. Graham Lescher and H. R. M. Richards. *Brit. J. Ven. Dis.*, London, 20: 37-41, Mar. 1944.

Twenty patients with neurosyphilis which had not reached the dementia paralytica stage were treated with malaria. Of these, 3 were of the congenital and 5 of the acquired meningovascular type, 10 were tabetic and 2 were tabetic with optic atrophy. The majority had not responded clinically nor serologically to tryparsamide or bismuth. The patients were carefully selected, all were well-nourished, and were free from infective or debilitating diseases. Special care was taken to exclude patients who had gross infection of the bladder or in whom there was evidence of damage to the cardiovascular, renal or hepatic systems. The method of administration was by the intravenous or intramuscular injection of 4 cc. of blood taken from a patient infected with benign tertian or quartan malaria. Further chemical treatment was given when considered necessary.

The most striking clinical improvement occurred in the congenital and acquired types of meningovascular syphilis. In the congenital type the most outstanding feature was the marked intellectual improvement which occurred soon after the termination of the infection, together with a diminution in number or cessation of the convulsions. These patients were able to assume responsible work within a reasonable time.

After combined malarial and chemical treatment, clinical improvement occurred and has been maintained in 15 patients, together with improvement in the condition of the cerebrospinal fluid and in the blood serum reactions.

**The treatment of acute gonorrhea in the Army.** Guy Campbell and George R. Carpenter. *Am. J. Syph., Gonor. & Ven. Dis.*, St. Louis, 28: 406-412, July 1944.

In a 10-months' period 3,270 patients with acute gonorrhea were treated with sulfonamides at Fort Bragg, N. C.; of these patients 2,100 were treated in the Station Hospital and 1,170 were treated on a

"duty status" basis. This study was made to report the results of treatment as directed by Circular Letter No. 74, issued by the Surgeon General of the Army on July 25, 1942. The treatment used was 4 gm. sulfathiazole daily for 5 days, one or more courses being given depending upon the response of the patient.

Of the 2,100 patients treated in the hospital, 1,714 (81.6 percent) recovered following one course of sulfathiazole, and 193 (9.2 percent) following a second course, giving a total recovery rate of 90.8 percent. Of the 1,170 patients given "duty status" treatment, 873 recovered following the first course and 216 following a second course. Of the entire group treated, 79.1 percent recovered following a single 5-day course of 20 gm. sulfathiazole and 12.5 percent following a second similar dose, giving a total recovery rate of 91.6 percent. There were 10 percent recurrences in the hospital treated cases.

No significant difference in results was noted between the hospital treated and the "duty status" treated groups of cases receiving the same dosage of sulfonamide drugs. The advantages of the latter are the reduction of days lost from military duty and the saving in hospital beds.

The drug reactions occurring in this series were few and not significant. The small number of patients developing complications was attributed to the fact that no local treatment was given on "duty status."

The results achieved in these groups of patients treated chiefly by medication show that acute gonorrhea, from a therapeutic standpoint, is a medical and not a urologic disease.

**Sulphonamide allergy.** R. G. Park. *Brit. M. J.*, London, No. 4353: 781-783, June 10, 1944.

Forty cases of both internal and eczematous allergy were investigated by skin tests and oral medication with various sulfonamides, sulfanilic acid, and procaine. Reactions in the eczematous cases consisted of a local flare-up plus a general dermatitis, starting in about 6 hours, and, in the internal cases, of pyrexia starting in about 2 hours. The skin test used in the eczema-

tous cases was a modified scratch technic with 50 percent pastes of powdered sulfonamides in hydrous lanolin and a 2 percent lanolin paste of procaine. The final method evolved was that of applying to one long scratch 4 different test materials on pieces of cloth about an inch apart, covering for 48 hours. The positive reaction was seen on that part of the scratch in contact with the irritating substance only. For oral testing the various sulfonamide drugs were used, giving an initial dose of 0.5 gm. and if no reaction appeared, increasing to 1 gm. every 4 hours for 48 hours.

The results showed 24 (60 percent) persons to be allergic to one sulfonamide drug only; 16 (40 percent) reacted to multiple sulfonamides and to sulfanilic acid.

**The use of sulfathiazole as a prophylactic agent.** James O. Gooch and Alvin L. Gorby. *Mil. Surgeon*, Washington, 94: 339-344, June 1944.

Sulfathiazole has been used as a prophylactic agent in the Armored Force at Fort Knox, Ky., since September 1942. Three plans of administration were tried: One in which 2 gm. of sulfathiazole were given every enlisted man going on pass and upon his return; the second method was not to give sulfathiazole upon departure but to administer 2 gm. upon return, repeating the 2 gm. dose 4 to 6 hours later; the third was the same as the second method, except that a 1 gm. dose was used. The men were encouraged to report to the prophylactic stations as soon as possible, emphasizing that the sulfathiazole was an adjunct to prevention of gonorrhea and was in no way a prevention against syphilis. Sulfathiazole prophylaxis was given to 6,998 men; the toxic manifestations noted were headache and dizziness in 2 cases, and slight nausea in 1.

At the time of instituting sulfathiazole prophylaxis the gonorrhea rates of the units averaged 170 per 1,000 a year. After 2½ months of application the rate was reduced to an average of 70 per 1,000 a year. The prevailing rate is due largely to cases contracted on furloughs and men transferred into the unit.

Various other plans of prophylaxis to test the efficiency and desirable dosage of sulfathiazole were tried out on 5,902 men who acknowledged exposures.

From these findings, sulfathiazole is considered an effective gonorrheal prophylactic agent. A total dose of 2 gm. sulfathiazole appears as effective as twice that amount. There was a concurrent lowering of the common respiratory disease rate in those units placed on a mandatory sulfathiazole gonorrheal prophylaxis regime, and a lowering of the syphilis rate due to increase in the number of prophylactic treatments for syphilis which were given at the time of sulfathiazole administration.

**Sulfathiazole for the prevention of gonorrhea.** Paul G. Reque and Daniel Bergsma. *Bull. U. S. Army M. Dept., Carlisle Barracks*, No. 78: 97-102, July 1944.

The authors report their findings on the effectiveness of sulfathiazole in the prevention of gonorrhea in a group of 5,037 men in the Army field forces under conditions of military training and alert status activity.

Each man was given a single dose of 3 gm. sulfathiazole within 2 hours after exposure, and routinely after the second hour. In 1,482 men who received sulfathiazole only, 1 (0.07 percent) failure was reported. In 3,555 who received sulfathiazole in addition to some other prophylaxis, 2 (0.06 percent) failures were reported. A total of 3 (0.06 percent) failures was found in the 5,037 men. In 191 (3.8 percent) minor reactions occurred.

The authors are of the opinion that sulfonamide prophylaxis is practical in field troops.

**Specific reactions occurring in the treatment of lymphogranuloma venereum with immune animal serums.** F. Sager. *Brit. J. Ven. Dis.*, London, 20: 55-60, June 1944.

Experiments were carried out with the use of animal convalescent serum in the treatment of lymphogranuloma venereum. Pus obtained from a patient suffering from lymphogranuloma venereum was injected into sheep and rabbits. Sheep were inocu-



lated intravenously with an injection of 1 cc. of pus diluted in saline in the proportion of 1 : 7; after 10 days this was followed by 1 cc. of pus diluted in the proportion of 1 : 4; after another 10 days the same amount diluted in the proportion of 1 : 2 was given. Rabbits were given (a) 0.5 cc. of pus intravenously in dilution 1 : 7; (b) 3 injections of 0.5 cc. each of pus in dilution 1 : 7 at intervals of 5 days; (c) 6 injections of pus in dilution 1 : 7 at similar intervals. During the subsequent 9 months the animals did not develop any clinical symptoms.

Two patients with lymphogranuloma venereum were treated with serum derived from the rabbits. They showed violent shock reactions. These same patients proved innocuous to normal rabbit serum. Sheep serum obtained in a similar manner provoked no ill effects.

From these findings the author concludes (1) that injections of 10 to 20 cc. of serum from rabbits inoculated with pus from patients suffering from lymphogranuloma venereum provoked grave and nearly fatal reactions in patients suffering from this disease; (2) that serum derived from immunized sheep provoked no reaction; (3) that a similar amount of serum from normal rabbits did not provoke any ill effects.

The author explains this peculiar phenomenon by stating that the effects seen could be a direct result of the use of serum of the animals previously inoculated with pus from lymphogranuloma venereum patients. It might be supposed that in the rabbit a dormant infection had been provoked into activity and had rendered the serum capable of producing the serious symptoms in the patient to whom it was subsequently administered. If it were possible to identify in the animal specific antigens by means of the complement fixation test this would be evidence in favor of such an assumption. In this way a latent infection in the animal might be proved, as it has already been proved for the human subject by Shaffer and his coworkers.

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## PATHOLOGY

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**Acute encephalopathy during neoarsphenamine treatment.** A report on six cases. W. A. Young and S. Gordon. Brit. J. Ven. Dis., London, 20: 34-36, Mar. 1944.

The authors conclude that the occurrence of 5 deaths from acute encephalopathy following about 10,000 injections at an East African center demands a reconsideration of the rather heavy dosage of neoarsphenamine which has been their routine. The routine dosage was 2 weekly injections of 0.6 gm. neoarsphenamine and 2 weekly injections of 0.1 gm. bismuth metal. A rise of temperature and injection of the conjunctivas were the most frequent reactions seen. In some instances the dose was reduced to 0.3 gm. neoarsphenamine or simultaneous injections of adrenalin were administered.

The 5 fatal cases of arsenical encephalopathy showed a striking conformity to a pattern. Within 12 to 48 hours of the administration of the last neoarsphenamine injection, sometimes as early as the third injection, sometimes as late as the fifth, the patient had an epileptiform attack, became quickly comatose and died within 24 to 48 hours. The initial convulsion was a frequent manifestation, although 1 patient remained drowsy after the last injection and then lapsed into a slowly deepening coma and another had transitory convulsions.

When the comatose state set in the patient appeared only semiconscious; he made unsuccessful attempts to reply to questions and resented being touched. The pupillary and other reflexes at first remained normal. Several patients were restless but later they lapsed into deep coma. One of them walked into the treatment room and fell upon the floor in convulsions.

These patients did not respond to adrenalin or venesection, and only temporary improvement was seen with lumbar puncture. They gave no evidence of a coincident infection with lymphogranuloma venereum.

A sixth patient with acute encephalopathy who had received continuous intravenous

administration of neoarsphenamine recovered.

Typical necropsy findings were edema and numerous petechial hemorrhages of the whole brain, slightly larger hemorrhages in the pituitary gland, cloudy swelling of the liver and congestion of the heart, kidney and alimentary canal.

**Aneurysm of the aorta rupturing into the right ventricle.** William H. Harris, Jr., and Herbert J. Schattenberg. *Ann. Int. Med.*, Lancaster, 20: 961-970, June 1944.

Rupture of syphilitic aneurysms of the aorta into the right ventricle is of rather rare occurrence. The authors report a case showing this complication and allude to 3 other cases from the literature.

A Negro, 61 years old, came into the hospital in January 1940 for the removal of a lipoma from his arm. At that time no cardiorespiratory involvement was noted, but blood tests were strongly positive for syphilis. He returned to the hospital on Apr. 10, 1942, complaining of dyspnea and retrosternal pain, both of which were of about a year's duration. An aortic aneurysm was considered, and when on Apr. 13 the retrosternal pain was suddenly accentuated, it was believed a rupture had occurred. The patient died within 3 hours. Autopsy gave a diagnosis of aneurysms of the aorta (intrapericardial portion and sinuses of Valsalva) with rupture into the right ventricle; cardiac hypertrophy and dilatational syphilitic aortitis. The largest aneurysm was a saccular one which arose 3 to 4 cm. above the aortic valve cusps. Since the right coronary artery could not be identified in this case, the possibility that the aneurysm may actually have had its origin from or, at least, bulged into this vessel was suggested. Syphilitic aneurysms of coronary arteries do occur and the site of the aneurysmal sac in this case was definitely above the site of the ostium of the right coronary.

## LABORATORY RESEARCH

**Stability of penicillin solutions at room and incubator temperatures.** William M. M. Kirby. *J. A. M. A.*, Chicago, 125: 628-629, July 1, 1944.

Studies were made relative to the deterioration of penicillin when kept at room and incubator temperatures. Preparations of the sodium salt of penicillin were diluted to 1.0 unit per cubic centimeter in isotonic solution of sodium chloride. Each lot was divided into three portions, one of which was kept at room temperature (about 22° C.), one in the incubator (37° C.) and one in the refrigerator (2° C.). Daily titrations of the activity of the various preparations were made.

There was no evidence of deterioration of any of the preparations kept at room temperature during the first 7 days, and most retained their full potency for 10 to 12 days. The preparations kept at refrigerator temperature showed no deterioration before the fourth day, but thereafter it was fairly rapid, all activity having disappeared usually after the eighth day. An experiment with the modified Rammelkamp dilution test, performed with freshly diluted penicillin and with the solutions which had stood at 2°, 22°, and 37° C. for 8 days showed the end point was the same at 2° C. and 22° C. as it was with the freshly diluted penicillin, indicating that no deterioration had occurred in the refrigerator or at room temperature. At 37° C. no penicillin activity remained.

These findings are of considerable clinical significance, as 1 or 2 days' supply can be mixed and left at the patient's bedside without danger of deterioration.

**The toxicity and treponemicidal activity of amide-substituted phenyl arsenoxides and their derivatives.** Harry Eagle, Ralph B. Hogan, George O. Doak and Harry G. Steinman. *J. Pharmacol. & Exper. Therap.*, Baltimore, 81: 142-150, June 1944.

A series of phenyl arsenoxides was pre-



red in which an acidic substituent group had been blocked by amide formation. Thirteen of these amide-substituted phenyl arsenoxides ( $-RCONH_2$ ,  $-RSO_2NH_2$ ) were, per unit arsenic, only 4.5 to 13.5 percent as toxic as the parent phenyl arsenoxide. Hence the treponemicidal activity in vitro was not reduced to the same degree, the ratio of treponemicidal activity  $\div$  toxicity was 1.9 to 6.1 times more favorable than that of phenyl arsenoxide. The favorable effect of amide groups was confirmed for all of these compounds by assays of toxicity and therapeutic activity in syphilitic rabbits.

When one or both of the amide hydrogens were substituted (e.g.,  $-SO_2N(CH_3)$ ,  $-ONH$ -pyridine), the effect of the entire group shifted toward that of the terminal substituent. In most cases, substitution in the amide therefore caused an increased toxicity, and impaired the favorable effect of the amide group as such. Only in the case of the compounds with terminal hydroxyl acetamido or nitrile groups was the favorable effect of the amide altogether preserved, perhaps because these groups in themselves depress the toxicity of phenyl arsenoxide.

The regularity with which substituents containing terminal amide groups decreased toxicity and increased the chemotherapeutic index of phenyl arsenoxide suggests that some members of this series may be of clinical utility.

**The effect of fever on the distribution of arsenic in the tissues of rabbits injected intravenously with mapharsen.** H. E. Stokinger, F. L. Dorn, R. A. Boak and C. M. Carpenter. *Am. J. Syph., Gonor. & Ven. Dis.*, St. Louis, 28: 465-470, July 1944.

The authors present their findings of a study made to determine whether a relationship exists between the distribution of arsenic in the tissues and the enhanced therapeutic efficacy and toxicity of the compound. A comparison was made of the arsenic present in tissues of rabbits (1) administered mapharsen only, (2) treated with mapharsen and fever, and (3) treated with mapharsen and fever but hydrated dur-

ing the fever to compensate for loss of fluids.

Observations were carried out on 30 rabbits, ranging in weight from 1.8 to 2.5 kg. Groups of 3 rabbits each were injected intravenously with 6.0 mg. mapharsen (maximal tolerated dose) per kilogram of body weight. One received no further treatment. Two were subjected to a fever at 41.5°C. for 3 hours immediately following the drug; 1 of these received in addition 3 periodic injections of warmed 0.85 percent solution of sodium chloride. Animals from each group were killed 3.5, 5, 15 and 24 hours after the injection of mapharsen.

The findings showed that there were significantly higher concentrations of arsenic in the tissues of rabbits treated with mapharsen and fever than in those treated with mapharsen alone. No significant difference was observed in the tissues of those animals dehydrated from those maintained at constant weight by hydration. Of the 12 tissues analyzed, the spinal cord and kidney showed the greatest increase in arsenic content after fever treatment. The blood levels were higher and the total arsenic content of the bladder urine was lower in the groups subjected to fever.

Less arsenic was present in the tissues 5, 15 and 24 hours after treatment than was observed at 3.5 hours, although the distribution was approximately the same. Observations made 24 hours after administration of the drug revealed the most marked differences in the concentration of arsenic in the three groups. Significant amounts of arsenic were still present in all the tissues in the fever-treated group, while in the other group only negligible amounts could be detected in the tissues other than the kidney and the lung. The kidney contained more arsenic at 24 hours than at any other period.

In discussing these findings the authors state that the greater concentration of arsenic in the tissues of rabbits subjected to fever following mapharsen may account for the enhanced therapeutic action of the drug and may be a factor in its increased toxicity. The findings suggest that fever may either bring about an increased deposi-

tion of the drug in the tissues or fix it more firmly, thus delaying elimination. The two factors may be involved simultaneously.

**The use of splenectomized and non-splenectomized mice in the production of experimental syphilis in rabbits.**

Udo J. Wile and Sture A. M. Johnson. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, **28**: 422-430, July 1944.

Because of differences of opinion as to whether the organism of syphilis can be demonstrated in mouse tissues, the authors experimented with white mice to determine (1) their usefulness as carriers of syphilitic infection and (2) whether or not after inoculation the organism of syphilis survives as such or whether there is suggestive evidence that it exists in an infravisible form.

The Nichols' strain of spirochetes obtained from rabbits was inoculated into three groups of mice, one intraperitoneally, the second intracranially, and the third intracutaneously by producing a marsupial pouch in the inoculated animals. Similar inoculations were given a group of splenectomized animals.

Six-week-old albino mice of Swiss strain, kept at a constant temperature of 70° F. in an air-conditioned room, were fed a complete mouse ration in pellet form. They were separated according to sex and experiments carried out with regard to the animal's sex in order to determine whether this was or was not a factor in the susceptibility of the animal.

The authors successfully produced experimental syphilis in rabbits using the brains, gonads, livers and spleens of white mice which had been inoculated with Nichols' strain of spirochetes obtained from rabbits. No difference was seen between splenectomized or nonsplenectomized animals, nor between male or female animals. In no instance in a large series of animals observed were any spirochete forms found either by darkfield examinations or by tissue staining in the mouse inoculums transferred to rabbits. Pathologic changes indicative or suggestive of syphilis were not found in any of the mouse tissues examined

and the mouse blood serologic Kahn tests were negative. The response in rabbits from inoculated mouse material was more striking than that observed in syphilis transferred from rabbit to rabbit, and in many instances the serologic titer was much higher by the former method. Control experiments with normal mice were consistently negative.

These experiments indicate that mouse tissue does not react to the *Spirochaeta pallida*. The uniformity of successful transfer from mouse tissue to rabbits suggests that the organism exists in the mouse host in a nondemonstrable form and that by passage through mice its virulence for rabbits is increased.

**The source of sulfathiazole hematuria induced in rabbits.** Gordon I. Trevett and S. S. Blackman, Jr. *Ann. Int. Med.*, Lancaster, **20**: 971-980, June 1944.

Hematuria was induced in 20 rabbits by the peroral administration of sulfathiazole. With one possible exception, adequate source for the blood was found in hemorrhages in the renal pelves, ureters or bladder. The apparent explanation of these hemorrhages is trauma from the precipitated drug crystals. In support of this hypothesis, crystals were frequently seen penetrating the mucosa at the site of hemorrhage, and in some instances a collection of crystals was closely adherent to the hemorrhagic area. A few large, collecting tubules in 4 of the 22 treated animals and in 7 of the 14 controls contained a few red blood cells. In none of the kidneys was there any evidence to indicate that sulfathiazole had injured the glomeruli.

Rabbits having an alkaline urine from eating Rab-ets developed hematuria from sulfathiazole less readily than did animals with an acid urine from oats.

**Production of vitamin K deficiency in rats by various sulfonamides.** A. Kornberg, F. S. Daft and W. H. Sebrell. *Pub. Health Rep.*, Washington, **59**: 832-844, June 30, 1944.

Postmortem examination to determine



the production of vitamin K deficiency in rats by the various sulfonamides were performed on 2 groups of albino rats, one group fed on an experimental diet of glucose ("Cerelese") 72 percent, casein 18 percent, cod liver oil 2 percent, cottonseed (Wesson) oil 3 percent, salt mixture No. 550, 4 percent, and one of the sulfonamides at a 1 percent level, and another group fed on an identical diet except that the sulfonamide drug was replaced by an equal weight of glucose.

It was found that sulfapyrazine, sulfadiazine or sulfathiazole fed to rats at a 1 percent level in purified diets resulted in a regular production of severe hypoprothrombinemia and hemorrhage in 2 to 3 weeks. Sulfaguanidine, sulfanilamide and succinylsulfathiazole were much less effective. Rats with hypoprothrombinemia induced by sulfapyrazine, sulfadiazine and sulfathiazole gave uniformly rapid and consistent responses to the oral administration of vitamin K (2-methyl-1, 4-naphthohydroquinone diacetate). The prothrombin level was found to attain a maximum by 10 hours after administration and no further increase was observed between 10 and 24 hours. The responses were independent of the rapidity with which the hypoprothrombinemia was produced and the sulfonamide which produced it. Five micrograms or more of the diacetate uniformly restored the prothrombin levels to normal values. A method for assay of the vitamin K activity of crude substances is presented.

Feeding experimental diets containing sulfadiazine or sulfathiazole was found to produce a severe hypoprothrombinemia, prolonged clotting time and multiple hemorrhages. These conditions were prevented by the oral administration of vitamin K.

Crystalline biotin and crystalline folic acid, alone or combined, did not influence the production of vitamin K deficiency by sulfadiazine.

The type of casein in the diet was found to be an important factor in the production of vitamin K deficiency. Alcohol extracts of leached casein showed vitamin K activity.

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## PUBLIC HEALTH ADMINISTRATION

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**Neurosyphilis treatment and disposition centers.** Bull. U. S. Army M. Dept., Carlisle Barracks, No. 78: 20, July 1944.

According to a recent War Department Technical Bulletin (TB MED 48) a program is set up for the management of neurosyphilis in the Army. Following the diagnosis, which is made in the field, all soldiers with neurosyphilis of any type are transferred to designated general hospitals for diagnostic review and treatment.

Because of the relatively short duration of infection of most soldiers with syphilis, it is expected that most neurosyphilitic patients will be of the asymptomatic type in which the spinal fluid is abnormal and neither symptomatic nor physical changes indicative of neurologic involvement are apparent. Asymptomatic neurosyphilitic patients with minor spinal fluid changes who may be expected to respond relatively quickly to antisymphilitic therapy will be retained in military service but will be reclassified as temporarily unfit for duty overseas, according to W. D. Circular 100, dated Mar. 9, 1944. Asymptomatic neurosyphilitic patients with marked spinal fluid changes and those with all other types of neurosyphilis, will be separated from the service after optimum treatment.

Treatment of those neurosyphilitic patients who are to be separated from the service will be given for a period of 3 months, the preferred methods being malarial fever therapy, mechanical fever therapy and chemotherapy.

Those asymptomatic neurosyphilitic patients with minor spinal fluid changes who are retained in the service are returned to their units for continuation of therapy on a duty status. If the patient fails to respond to treatment in 6 months, he is transferred again to the center for fever therapy and separation from the service.

In case of separation from the service, a complete case record of each patient will be

forwarded to the U. S. Public Health Service in order that continued observation and treatment may be assured. This continued therapy and observation will be provided by civilian or Governmental agencies as the individual case may require.

**Venereal disease control in the military scene.** Julius R. Scholtz. *California & West. Med.*, San Francisco, 60: 283-287, June 1944.

The civilian and military venereal disease control programs are complementary and supplementary and represent integral parts of the whole program. A review of the accomplishments in the control of venereal disease in California covering the years 1938, 1939, 1940 and 1941 shows a decrease of 40 percent in early cases of syphilis. This indicates that the reporting by physicians has improved and testifies to the effectiveness of the control program for the civilian population. Army reports for the years 1940 and 1941 indicate that the 9th Corps Area (which includes California) is far below the Army as a whole. From these findings it is seen that a close-working relationship has been established between civilian and military control programs. The general practitioner plays an important role in the control of venereal disease. About 50 percent of the cases of early syphilis and the majority of cases of acute gonorrhea are first seen and treated by him. Therefore, the management of the early case of venereal disease, from the standpoint of epidemiology and treatment, is the point of convergence of the efforts of the three forces for control—the military, the health departments, and the physician.

One of the weak points in the present program on the control of venereal disease is the lack of hospital facilities for infectious persons. Another is the lack of prophylactic stations in civilian areas, especially in the larger cities in the State where exposure most often takes place.

**Venereal disease.** *Indust. Med.*, Chicago, 13: 530, June 1944.

U. S. Public Health Service reports indicate that from 0.5 to 10.5 percent of in-

dustrial workers are infected with venereal disease. Federal expenditures for venereal disease control in the fiscal year 1943 totaled \$12,500,000 as compared with \$62,255 in 1935. The program for venereal disease control in industry is carried out in co-operation with the Division of Industrial Hygiene of the U. S. Public Health Service and 38 State industrial hygiene organizations. These agencies offer consultation service to industry.

In 1943, a total of 1,488,868 industrial workers were tested for syphilis, with 31,657 (2.1 percent) found to be infected. Of this number 4,365 were already receiving treatment, 8,009 were placed under treatment, and 15,774 were investigated to trace infected contacts.

The program to be developed in 1944 is based on the recommendations of an Advisory Committee appointed by the Surgeon General in 1942 to study venereal disease control in industry. The recommendations have been accepted by management, labor, the medical profession, and public health authorities.

**Venereal disease control in industry.**

An address before the New Jersey Association of Industrial Physicians, November 12, 1943. Glenn S. Usher. *J. M. Soc. New Jersey*, Trenton, 41: 234-238, June 1944.

From a recent sampling survey it was found that of 80 industrial plants in New Jersey, 54 performed pre-employment physical examinations and in only 33 of these were routine blood tests included; 23 examined men for gonorrhea and only 5 examined women employees for gonorrhea. Twenty of these plants conduct periodic physical examinations and in only 7 of these is the blood test included. In 25 of the industrial plants the employees are given medical examinations upon return from absence.

Regarding the employment policies of these 80 plants: In 24 it was the policy to discharge employees who are found to have infectious syphilis, 10 of these discharging employees even if the syphilis is found to be latent. In 17 plants employees found to have gonorrhea are discharged. Twenty-



eight plants have the policy of rejecting applicants for syphilis regardless of the stage of the disease and 42 reject applicants with gonorrhea. In 17 of these plants the records are not confidential.

The author feels that industrial medicine in New Jersey is not taking full advantage of its opportunities in a field in which it can be of great service both in maintaining war production and in protecting the health of industrial workers and their families. He points out the value of an educational program and a venereal disease control program in industry and the benefits derived from these efforts.

**Pre-marital certificates.** Editorial. California & West. Med., San Francisco, 60: 277, June 1944.

Premarital certificates may not be issued in California by drugless practitioners, including chiropractors, because State law limits such authority to duly licensed physicians and surgeons. This statement was made in opinion NS5326 by the Attorney General in reply to a request for a ruling made by the Director of Public Health. Only those licensed by the Board of Medical Examiners and the Board of Osteopathic Examiners may legally issue such certificates. A county clerk would be guilty of a misdemeanor if he accepted a pre-marital certificate not made out by a "duly licensed physician or surgeon."

**A synopsis of laboratory diagnosis in gynecology.** Editorial. South. Med. & Surg., Charlotte, 106: 208-209, June 1944.

Since cases of gonorrhea in the female may have a potential medicolegal angle and the courts of many States are now demanding the result of a culture, this method of examination should be made in every questionable case. Before any woman is committed to a State detention institution as a gonorrhea victim, culture should prove the diagnosis.

Any patient having an intractable vaginal discharge in which gonococci cannot be demonstrated should be examined for trichomonads. The diagnosis can be made in a few seconds and treatment instituted

immediately. If it is necessary to send the specimen to the laboratory for examination, these organisms may be kept alive for 30 minutes on a swab which is immersed in normal saline at 99° in a test-tube and kept at that temperature until it reaches the examiner.

In *Trichomonas vaginalis* the secretion has a yellowish-green color with a tendency to be foamy. Punctuate, superficially ulcerated areas are seen by the aid of the speculum on the cervix and vault. A drop of the material is placed upon a slide and a cover-glass applied. The high-dry lens facilitates diagnosis but the rapidly moving organisms can be seen under the low power. Nonmotile organisms are more difficult to identify.

**Ministry of Health standardizes tests of recovery from venereal diseases.** London correspondent. J. A. M. A., Chicago, 125: 804, July 15, 1944. Also: Lancet, London, 1: 741-742, June 3, 1944.

The Ministry of Health has issued a memorandum for medical officers specifying the tests which should be employed before discharging persons who have had syphilis or gonorrhea.

In cases of gonorrhea, the blood should be examined a week after treatment has been stopped and monthly thereafter for a minimum of 3 months for the serum reactions. Men should be instructed concerning taking spreads of any urethral discharge. A week after suspending treatment the early morning urine or urine held for 4 hours should be examined after an attempt to obtain discharge at the meatus. Any thread or discharge should be examined bacteriologically. Specimens of prostatic and vesicular secretion should be microscopically examined. Cultures of secretions are also desirable. If no evidence of persisting infection is obtained, the urethra should be filled with a provocative solution and retained for over 2 minutes. The prostate and seminal vesicles should be massaged after the bladder has been emptied and the secretion left in the urethra. If no evidence of relapse is obtained, these measures should be repeated

weekly for 1 month and thereafter monthly for two or more times. The anterior urethra should then be examined with a urethroscope and a full-sized metal sound passed into the bladder. These manipulations may produce a discharge, of which the patient should obtain a specimen.

In the case of women, a week after suspending treatment specimens should be taken from the urethra, cervical canal and rectum and examined in stained spread and culture. Specimens from the urethra and cervical canal should preferably be taken the day after painting with a provocative chemical. There should also be inspection of the orifices of the Bartholin and any paraurethral ducts and examination of spreads made from the expressed secretions. These procedures should be repeated weekly for a month and then monthly for 3 months, the specimens being taken just after menstruation if possible. Before final discharge, careful pelvic examination should be made.

In cases of syphilis, the blood should be tested every 3 months after completing treatment for the first year and every 6 months for the second year. The spinal fluid should be tested at the end of treatment or earlier if the blood reactions are resistant, and the test should be repeated at the end of 2 years of observation. These tests are regarded minimal for both sexes.

**Is a new deal in the control of venereal disease necessary?—I.** I. N. Orpwood Price. *Brit. J. Ven. Dis.*, London, 20: 19–21, Mar. 1944. Discussion pp. 25–30.

In an address before the Medical Society for the Study of Venereal Diseases, Nov. 27, 1943, the author pointed out some of the faults of the present scheme of venereal disease control. He feels that now is the time to formulate reforms which will raise the standard of this work and the status of those engaged in it, not only in wartime but also in the years to come.

The lack of interest and of support by most members of county councils and town councils, by health officers, by the medical profession and by the general public is a major fault of the present scheme. Other

points mentioned are the atmosphere of most venereal disease clinics, the poor laboratory facilities, the discouraging outlook of medical officers engaged in this work, and the effect of almoners in venereal disease clinics.

The author submits some suggestions which he feels will prove of value, among which is the formation of a small sub-committee to formulate a policy on the running of venereal disease clinics which, after the approval of the Society, will be forwarded to the Ministry of Health and local administrations. It is also suggested that a National Venereal Diseases Service be set up to be run by the local authorities through the Ministry of Health and supported by the central government. Appointments to the venereal disease service should be made by the central administration in conjunction with the local authorities, who are responsible for the running of the clinics in their area under the supervision of the Ministry of Health. The whole country should be zoned according to population and a requisite number of clinics provided. The medical staff should hold permanent appointments and should be able to meet specific qualifications of training in this work. The laboratories should be staffed by properly trained persons with special experience in the practice of venereal disease pathology.

**Prevention of congenital syphilis—I.** Nora I. Wattie. *Brit. J. Ven. Dis.*, London, 20: 61–65, June 1944. Discussion pp. 69–73.

The author, in an address to the Medical Society for the Study of Venereal Diseases, on Mar. 25, 1944, outlines the method of handling cases of congenital syphilis in Glasgow. The scheme which has been used since 1924 is based on the general principle that the venereal diseases in mothers and children should be treated where they are detected, whether at an antenatal clinic, a child welfare clinic or in a maternity hospital, and that the administration of treatment should be regarded as an integral part of maternity and child welfare. The success achieved in Glasgow is attributed to the fact that there



is no delay in treatment and that it is much easier to induce the pregnant woman to come for treatment to the ordinary antenatal clinic where no differentiation is made between herself and any other patient. Certain special sessions are set aside for the continued postnatal treatment and for the treatment of the child if necessary. In this way the patient continues to receive treatment from the same doctor and health visitor, and the place of treatment is the one to which she is accustomed. The medical staff is trained as both child welfare and venereal disease workers.

The Glasgow scheme of treatment and its results up to the outbreak of the war are a good example of a public health preventive measure applied successfully to a high proportion of the expectant mothers. In 1922 the number of congenitally syphilitic children observed who were under 1 year of age was 335, while in 1943 this number had decreased to 32, the lowest reported number for the intervening years being 15 children under 1 year of age in 1941. The congenital syphilis rate for infants less than 1 year of age reported for Scotland for the years 1931 to 1942, inclusive, shows a gradual and continuous decrease from 1.95 per 1,000 births in 1931 to 0.93 in 1942. The corresponding figures for England and Wales were 0.53 and 0.37, respectively.

With the outbreak of the war the problem of acute infection occurring in pregnancy due to promiscuity is of paramount importance. Its control is dependent upon the control of venereal disease as an infectious disease and strong support should be given to the notification of these diseases.

**The problem of venereal disease in the Transkei.** J. M. Tobias. South African M. J., Cape Town, 18: 142-144, Apr. 22, 1944.

Accurate data as to the extent of gonorrhea among the natives in the Transkei are not available. Statistics are presented, however, on the prevalence of syphilis.

For the year ending August 1943, there were 104 (8.8 percent) strongly positive, 32 (2.7 percent) positive, and 46 (3.8 percent) doubtful Wassermann reactions

among 1,184 patients at the Sir Henry Elliot Hospital, Umtata. Some of these tests were made routinely, others because syphilis was suspected. Out of a total of 57 cases at the St. Barnabas Mission Hospital, in which the Wassermann test was done routinely, the reactions were strongly positive in 10 (17.6 percent), positive in 1 (1.7 percent), and doubtful in 2 (3.5 percent). In the author's practice, the Wassermann test (the only test for syphilis employed) is done where syphilis is suspected. Out of 71 cases, 23 percent were strongly positive, 5 percent positive, and 7 percent doubtful.

In 1927 the Institute for Medical Research examined the blood of apparently healthy natives of 3 tribes in the Transkei and the findings were for the Basutos, 28 percent; for the Pondos, 7.8 percent; for the Xosas, 2 percent.

In January 1938, the author started the venereal disease clinic at Nkanga in the Libode District, where he is the Surgeon-in-charge. It is optional with the patient whether he remains in the clinic for treatment or comes as an outpatient. Compulsion was used only in exceptional cases. The course lasts 6 weeks. Neoarsphenamine is given intravenously in doses of from 0.3 gm. to 0.9 gm. (a total of 3.75 gm), and an injection of bismuth is given each week; infants are given acetylarsan. Potassium iodide is also given. In over a thousand cases, there was only one toxic reaction.

The clinic load increased from 121 patients (786 attendances) in 1939 to 466 patients (2,038 attendances) in 1943; 78 percent of the patients completed the 6 weeks' course. Refusal to treat a patient who would not attend the clinic regularly was more effective than other methods of compulsion. Outpatient service was preferred, only 6.6 percent remaining in the clinic; 34.7 percent of the female patients and 50.7 percent of the males came from districts outside of Libode.

The work of Bernstein, Assistant Medical Officer to the Consolidated Main Reef, is cited. In his series of cases, 3.6 gm. neoarsphenamine were given. After 3 months, 57.1 percent were negative and

after 6 months, 79 percent. The findings indicate that the Bantu yields better to treatment than Europeans and prolonged treatment is not needed.

The pathology that untreated syphilis creates in the African is discussed. Cases of aortic incompetence are rare; in 8 years, the author saw only 4 cases of aneurysm. Gummatous perforation of the palate is relatively common, and congenital syphilis is quite frequent. The author does not recall a single case of gonococcic stricture causing retention. From 1936-1940, 320 (7.8 percent) out of 4,071 male natives and 98 (5 percent) out of 1,865 female natives admitted to mental hospitals throughout the Union were suffering from cerebral syphilis, as compared with 1 percent in 1920. Corresponding figures for Europeans are 4.7 percent and for Negroes, 19.6 percent.

**Syphilis in Hawaii.** Hawaii M. J., Honolulu, 3: 229-230, May-June, 1944.

In a serologic survey among food handlers recently conducted by the Board of Health, 11,000 persons were given the standard diagnostic Kahn test; those with a positive reaction were given the Kolmer test as well. Of the group, 317 persons (2.92 percent) had positive reactions for syphilis. The rate in the urban district was 2.67 percent and in the rural, 4.72 percent. Of 150 seropositive food handlers questioned, 94 were not aware of their infection.

**Division of Public Health quarterly report: Jan. 1 to Mar. 31, 1944.** Department of Health of Puerto Rico. Puerto Rico Health Bull., San Juan, 8: 69-103, Apr.-June 1944.

During the 3-month period (Jan., Feb., Mar. 1944) syphilis occupied second place in the list of reportable diseases with a total of 2,359 (470.2 per 100,000 population), or an increase of 7.6 in the morbidity rate as compared with the same period of the previous year. There were 1,045 (209.1 per 100,000 population) cases of gonorrhea reported for the same period.

A study was made on 280 patients in the venereal disease isolation hospitals to determine the characteristics of this group

of patients and their possibilities for social rehabilitation. Another study was made of 238 cases which had received case-work and treatment in the public health units and district hospitals with a view of determining the medical social services given the patients, and of discovering any fundamental differences between services rendered in the public health units and in the hospitals.

The Bureau of Venereal Diseases reports its activities for the third quarter of the 1944 fiscal year and submits some comparative figures with the second quarter. A slight rise in the number of cases of gonorrhea, chancroid and lymphogranuloma venereum was reported by treatment sources in the third quarter. This is thought to be due to attempts of the Bureau of Venereal Diseases to enlist the cooperation of private practice treatment sources in reporting venereal disease. The activities of the venereal disease clinics show a decline for the third quarter, but since many of the clinics are delinquent in their reports an increase is expected for the fourth quarter. The average patient load and the number of treatments administered have risen sharply in the two rapid treatment centers at Caguas and Troche. This information is included in 3 tables.

**Proceedings of the Puerto Rico Regional Conference on Social Hygiene.** J. Social Hyg., New York, 30: 165-268, Apr. 1944.

The Regional Social Hygiene Conference held in San Juan, P. R., Feb. 9-10, 1944, was one of about 18 such conferences held in the United States and Canada in observance of National Social Hygiene Day. Dr. A. Fernós Isern, Insular Commissioner of Health, presided.

Participating organizations were the Puerto Rico Committee on Social Protection, the Health Department of Puerto Rico, the Division of Social Protection of the Federal Security Agency, the U. S. Public Health Service, and The American Social Hygiene Association, with the cooperation of the Medical Corps of the U. S. Army, Antilles Department, and the



U. S. Navy, Tenth Naval District, and 58 sponsoring agencies.

Speaking on the Army's campaign for venereal disease control, Maj. Gen. M. C. Stayer outlined effective Army-controllable factors and technics. Important among these are ruling out of punishment, which is replaced by exact knowledge and self respect as motivating influences, and an educational program. Each commanding officer is specifically responsible for the control of venereal diseases among the personnel under his command. A definite decrease in the Army venereal disease rates occurred in the Caribbean area during 1943, the total rate for January 1943 of 85 per 1,000 troops dropping to 38 in December 1943—a 55 percent decrease. Gratifying progress is shown in the Panama Canal area where the rate was 68 in January 1943 and 23 in December 1943, a drop of 71 percent.

Lt. Comdr. Frank W. Reynolds stated that the Navy's problem in venereal disease control was especially acute in the Caribbean area. In 1942 (the last year for which all the statistical data are available) the venereal disease rate for this area was higher than in any other Naval District, and 6 times as high as in the continental United States. During 1943, over 500 venereal infections were contracted by Navy personnel in San Juan, with over 10,000 man-days lost. In 1 year, the venereal disease control program reduced the rate by 50 percent. Further progress is considered chiefly dependent upon the civilian community.

R. A. Vonderlehr, Director, U. S. Public Health Service District No. 6, Puerto Rico, stated that the formal adoption by an interdepartmental venereal disease committee of a United States government policy on venereal disease control in the Caribbean in 1943 was an important measure. It charges the Public Health Service, the Pan American Sanitary Bureau, and the Anglo-American Caribbean Commission with the responsibility of stimulating the organization and operation of civilian services for venereal disease control by the respective insular Caribbean governments. The facilities and the services recommended

are: (1) Effective methods of diagnosis; (2) clinics operated in accordance with best scientific standards; (3) hospital facilities for the isolation of infectious patients; (4) qualified follow-up workers for contact-tracing and case-holding work, and (5) a modern program of public education.

Provision is being made in cooperation with the Anglo-American Caribbean Commission for the installation of a program of this kind on the Island of Trinidad. This, the first attempt at Anglo-American collaboration in a movement against the venereal diseases in the New World, will establish, with the joint financial support of both the United States and the British Government, an up-to-date venereal disease control program. Such a program is urgently needed in Trinidad and the other Antilles, not only for the health of the Armed Forces but for the civilian population as well.

Thomas Parran, Surgeon General of the U. S. Public Health Service, stated that the venereal diseases are a "number one" health problem and emphasized the urgent need for adequate laws and their vigorous enforcement. He pointed out that it is to the Social Protection Committee that the authorities will look for the creation of public sentiment and cooperation essential to any program of repression and venereal disease control in Puerto Rico. The problem in Puerto Rico parallels in many respects the situation in some of the Southern States. Recent estimates based on Selective Service findings show that Puerto Rico's prevalence rate of syphilis among young males is 120 per 1,000, which is somewhat higher than the 5 Southern States with the highest combined rates in the mainland (100 or more per 1,000). The Federal allotment to Puerto Rico for venereal disease control for 1944 is \$383,000, of which \$118,400 is for war-emergency control. Added to this are funds for an Island-wide system of rapid treatment. The number of venereal disease clinics in Puerto Rico increased from 13 in 1939 to 47 in 1943.

Dr. Fernós Isern said that Puerto Rico's task is to develop the program drawn up by the Committee on Social Protection, the

work being distributed among 5 subcommittees: (1) Education in Venereal Diseases; (2) Treatment of Venereal Diseases; (3) Legislation; (4) Law Enforcement, and (5) Rehabilitation.

**Syphilis morbidity in Madrid, social importance and collaboration of all physicians in the antivenereal disease campaign.** (Morbilidad de la sífilis en Madrid, importancia social y colaboración de todos los médicos en la lucha antivenerea.) *Semana méd. españ.*, Madrid, 6: 375-380, 1943. *Abs. Zentralbl. f. Bakt.*, Jena, 144: 269, 1944.

The prevalence of syphilis among the population of Madrid is 3 per 100; since the Civil War there has been a 100 percent increase in the number of cases of early, infectious syphilis, and the prevalence is increasing at an alarming rate. The Medical Surgical Academy has pointed out that the only way to combat this disease is by tracing sources of infection and by making treatment of infectious persons compulsory.

#### **The venereal diseases as cause of death.**

(Die Geschlechtskrankheiten als Todesursachen.) H. Gottschalk. *Deutsche med. Wchnschr.*, Leipzig, pp. 845-947, 1942. *Abs. Zentralbl. f. Bakt.*, Jena, 143: 337, 1943.

Official mortality statistics do not give complete information on mortality due to syphilis. More reliable statistics are the "Magdeburg combined morbidity statistics" for the period 1928-1936. These statistics include 8,182 dead for whom both the clinically determined cause of death and autopsy findings are available. Of this number 322 (3.9 percent) died as result of disease which was clinically diagnosed as syphilis; in 214 (66 percent) the clinical diagnosis was confirmed by autopsy findings. In another 192 cases the cause of death was determined at autopsy to have been syphilis, bringing the total number of causes of death due to syphilis to 406. By means of autopsy, therefore, 26 percent more cases in which death was due to syphilis were diagnosed than by clinical findings alone. In case of *tabes dorsalis* 63 percent

and in case of aneurysm 250 percent more cases were found by autopsy than by clinical examination. These two syphilitic conditions are therefore most frequently incorrectly diagnosed clinically.

#### **Studies on syphilis in Puerto Rico. III.**

**Survey based on the results of flocculation tests among 19,395 selectees and volunteers during the year 1941.** O. Costa Mandry and José L. Janer. *Puerto Rico J. Pub. Health & Trop. Med.*, New York, 19: 483-491, Mar. 1944.

In 1941 a total of 19,395 blood specimens were obtained from male volunteers and selectees in Puerto Rico and sent to the public health laboratories on the Island for examination. Of these, 18,603 proved satisfactory for flocculation tests, 12.3 percent giving positive Kahn reactions and 13.8 percent positive Kline reactions.

The percentage of positive Kahn reactions was found higher in the urban zone (15.6 percent) than in the rural zone (10.2 percent); for similar age and residence groups it was higher in the nonwhite (14.8 percent) than in the white (11.5 percent).

In the rural zone, the percentage of positive reactions was higher in the present study than in a similar survey of corresponding age groups made up of 7,453 male agricultural workers in 1934.

The positive serologic results were higher in the whites in Puerto Rico than in most States of continental United States but show a closer parallel with some of the Southern States. However, the percentage of positive serologic results among the nonwhites is much lower for Puerto Rico than for the United States as a whole or most of the Southern States.

**Committee on Syphilis Control.** (Louis G. Martin, Chairman.) *J. Arkansas M. Soc.*, Little Rock, 41: 18, June 1944.

This report of the Committee on Syphilis Control was presented at the 69th Annual Session of the Arkansas Medical Society held Apr. 17-18, 1944.

Included in a summary of the work done by the State Board of Health was the passage and adoption by the State



legislature of Act No. 240 to prohibit prostitution, lewdness and assignation. In addition, 84 diagnostic and treatment clinics were maintained and supervised by the State Board of Health throughout the State. The personnel comprised 1 full-time and 46 part-time clinicians. Three full-time U. S. Public Health Service venereal disease control officers directed control activities, under the supervision of the State Board of Health, in the large extra-military areas.

The total number of cases of syphilis of all stages reported during 1943 was 13,045, chancroid 105 cases, lymphogranuloma venereum 24, granuloma inguinale 73, and gonorrhea 3,305.

**Venereal disease control.** Roy L. Kile. Bull. Acad. Med. Cleveland, 29: 14, May 1944.

Over 5,000 cases of venereal disease were reported to the Cleveland Division of Health in 1943, 50 percent being from private physicians. The contact case-finding work done by private physicians is not satisfactory. An attempt is being made to work out a more satisfactory plan. The question of whether the physician shall investigate contacts among his private patients or whether the health department be asked to do so is an individual problem. Provision has been made whereby contacts can be reported on State Form OVD 26.

# New Cases of Syphilis and Gonorrhea in States, Territories, Possessions and Panama Canal Zone

Health officers' monthly statement: Reported for the fiscal years 1943-44 and 1942-43

Area	Cases of syphilis and gonorrhea reported for the fiscal years below											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital			
	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43
United States†	158,363	155,515	178,327	13,736	124,126	149,763	100,086	124,264	113,500	116,515	201,350	227,600
Alabama.....	17,653	21,114	2,188	3,260	4,027	5,836	4,318	6,166	383	509	6,561	8,000
Arizona.....	2,887	2,813	730	431	818	659	1,094	1,493	138	131	1,760	1,000
Arkansas.....	9,891	18,681	1,236	1,758	3,318	6,440	3,769	6,661	233	304	4,270	4,000
California.....	33,712	32,611	6,728	4,438	7,694	7,446	18,751	18,615	964	966	36,594	24,000
Colorado.....	3,741	5,271	904	1,019	1,070	1,334	1,629	2,654	138	234	3,185	2,000
Connecticut.....	2,932	2,893	325	250	1,303	926	718	989	143	106	1,531	1,000
Delaware.....	972	1,025	162	125	286	250	268	269	25	40	239	1,000
D. Columbia.....	8,261	7,003	1,070	809	1,968	1,866	4,867	3,321	130	125	4,234	3,000
Florida.....	26,978	35,055	3,091	4,192	8,734	9,105	12,193	17,127	576	825	16,063	14,000
Georgia.....	15,286	27,638	3,139	3,965	6,032	12,984	5,657	9,955	453	731	9,400	12,000
Idaho.....	665	450	229	166	132	36	249	200	23	20	840	1,000
Illinois.....	27,719	29,620	3,698	3,353	6,109	6,214	17,315	19,328	597	735	22,989	20,000
Indiana.....	8,377	12,770	1,254	1,674	867	465	3,044	5,000	249	401	3,307	4,000
Iowa.....	2,365	2,849	468	386	608	895	1,045	1,264	142	102	1,815	1,000
Kansas.....	2,868	4,053	594	772	603	578	1,563	2,075	108	118	1,858	2,000
Kentucky.....	6,673	12,530	1,065	1,532	1,454	2,787	2,839	5,386	274	410	3,770	4,000
Louisiana.....	17,500	19,094	3,123	2,608	4,599	5,727	4,680	8,376	469	570	14,007	8,000
Maine.....	1,067	1,042	226	226	149	174	536	462	98	98	1,418	1,000
Maryland.....	13,149	19,352	1,671	1,387	2,059	1,572	2,893	2,452	131	213	6,557	8,000
Massachusetts.....	5,631	5,578	1,148	1,028	(8)	(8)	4,137	4,272	344	276	5,068	4,000
Michigan.....	17,486	14,088	2,531	1,909	4,718	3,124	7,460	6,364	455	478	11,349	8,000
Minnesota.....	2,419	2,955	234	237	282	325	1,737	2,213	116	106	1,961	1,000
Mississippi.....	25,867	38,002	8,769	9,691	7,300	12,715	8,566	14,085	1,148	1,511	30,351	32,000
Missouri.....	10,427	8,842	1,844	1,400	2,660	1,722	5,108	4,240	352	238	6,412	4,000
Montana.....	435	475	108	157	63	34	165	226	7	11	296	1,000
Nebraska.....	1,378	1,945	209	225	557	538	526	1,000	38	64	1,393	1,000
Nevada.....	813	767	83	1	101	138	546	481	27	14	409	1,000
New Hampshire.....	295	319	45	35	56	28	158	218	21	23	195	1,000
New Jersey.....	10,888	10,966	1,317	1,314	3,200	2,955	5,864	6,214	423	372	5,284	6,000
New Mexico.....	2,009	2,352	414	411	478	556	1,021	1,246	86	120	1,405	1,000
New York.....	35,500	37,793	5,387	4,070	6,490	5,877	22,248	26,588	997	1,255	19,104	16,000
North Carolina.....	11,115	17,243	3,100	3,666	4,409	7,305	3,382	5,867	204	405	9,660	11,000
North Dakota.....	312	325	96	42	55	59	88	143	23	19	265	1,000
Ohio.....	23,276	23,500	3,779	3,437	5,738	5,535	12,066	13,523	912	1,005	5,775	4,000
Oklahoma.....	8,027	11,070	1,109	1,594	2,180	4,051	2,922	2,932	301	349	5,337	4,000
Oregon.....	(*)	1,410	(*)	277	(*)	118	(*)	999	(*)	69	(*)	1,000
Pennsylvania.....	13,421	8,156	1,751	1,261	4,785	4,235	4,887	1,795	637	215	(*)	(*)
Rhode Island.....	1,078	1,131	142	52	113	92	661	855	24	41	999	1,000
South Carolina.....	15,410	20,286	3,267	4,300	5,932	8,552	5,523	6,621	350	433	6,135	6,000
South Dakota.....	461	508	106	105	90	162	229	185	34	23	357	1,000
Tennessee.....	19,720	23,813	2,373	2,995	7,609	8,271	8,063	11,720	434	576	13,093	11,000
Texas.....	24,194	45,687	3,407	5,615	7,490	10,015	9,777	15,265	808	1,597	11,472	15,000
Utah.....	824	714	202	270	115	90	489	387	18	13	681	1,000
Vermont.....	266	276	78	127	84	15	91	117	12	17	212	1,000
Virginia.....	15,701	17,766	4,136	5,313	6,078	6,481	5,043	5,377	263	388	12,476	8,000
Washington.....	4,050	3,720	815	770	879	622	1,816	1,874	120	117	7,066	5,000
West Virginia.....	3,535	5,395	646	858	555	924	829	1,447	114	173	2,369	2,000
Wisconsin.....	906	1,098	186	208	0	1	711	869	9	21	1,062	1,000
Wyoming.....	1,073	671	124	164	179	47	525	257	29	17	186	1,000
Territories, Possessions, and Panama C. Z.												
Alaska.....	100	158	54	48	16	41	18	38	1	7	448	1,000
Hawaii.....	994	1,104	212	277	102	136	638	540	65	68	1,784	1,000
Puerto Rico.....	14,410	9,694	1,605	2,021	2,764	1,523	4,785	3,288	2,057	1,685	4,216	3,000
Virgin Islands.....	182	229	27	58	107	125	39	30	8	9	252	1,000
Canal Zone.....	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)
Actual total† of U. S. and Territories and Canal Zone...	474,049	572,110	80,225	86,417	127,115	151,706	207,566	253,109	15,711	18,353	308,050	283,000

\* Data not available.

\*\* Includes "not stated."

† Based on States reporting in both fiscal periods.

‡ Included in late and late latent.

† Includes all reported cases

‡ Based on 48 States.

‡ Based on 47 States.



# New Cases of Syphilis and Gonorrhea in Cities of 200,000 and Over

Health officers' monthly statement: Reported for the fiscal years 1943-44 and 1942-43

City	Cases of syphilis and gonorrhea reported for the fiscal years below											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital		1943-44	1942-43
	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43	1943-44	1942-43		
Total†	150,967	159,954	18,925	17,828	35,071	31,455	69,299	77,779	3,071	3,363	78,097	68,579
Kron.....	886	1,284	137	179	197	248	490	799	48	58	352	268
Atlanta.....	2,653	4,082	670	891	822	1,508	1,246	1,642	26	41	1,590	1,031
Baltimore.....	9,808	15,353	1,282	1,048	1,275	1,090	2,311	1,877	70	83	2,588	3,885
Birmingham.....	4,697	6,266	314	510	1,213	1,829	1,233	1,636	83	145	555	852
Boston.....	1,852	2,067	355	323	0	147	1,182	1,331	56	80	1,379	1,223
Buffalo.....	1,962	1,910	222	158	222	93	1,472	1,588	46	71	917	993
Chicago.....	16,434	16,981	2,466	2,316	3,680	3,630	9,932	10,617	356	418	13,343	13,005
Cincinnati.....	(*)	3,693	(*)	430	(*)	(*)	(*)	(*)	(*)	0	(*)	995
Cleveland.....	4,473	4,054	859	687	1,424	1,000	2,094	2,230	96	137	1,599	1,397
Columbus.....	1,601	1,599	341	215	365	337	829	985	46	62	345	380
Dallas.....	2,547	3,216	506	440	554	589	1,466	2,151	19	34	795	1,091
Dayton.....	1,650	1,311	180	176	457	264	958	826	55	41	631	277
Denver.....	1,783	2,250	407	436	500	449	656	1,255	53	54	1,631	1,227
Detroit.....	11,875	9,511	1,545	1,203	3,806	2,352	6,299	5,753	225	203	5,782	5,132
Honolulu.....	528	661	68	217	62	91	347	310	46	43	1,120	1,082
Houston.....	1,956	4,179	362	319	691	1,378	843	2,377	60	105	2,212	1,282
Indianapolis.....	2,272	3,777	509	624	119	73	546	859	30	32	163	436
Jersey City.....	468	689	47	58	97	121	312	490	22	30	49	47
Kansas City.....	1,854	1,962	306	287	343	262	1,106	1,233	79	84	1,005	934
Los Angeles.....	11,634	10,547	27	766	4,654	3,005	6,642	6,438	311	288	5,276	4,778
Louisville.....	1,960	2,420	351	298	369	437	855	1,447	35	57	1,020	1,201
Memphis.....	7,699	8,069	608	654	3,588	3,076	3,374	4,111	106	110	5,146	3,342
Milwaukee.....	499	561	66	77	13	5	402	472	5	7	219	104
Minneapolis.....	714	830	115	87	133	135	440	588	23	21	764	666
Newark.....	2,130	2,404	315	319	584	681	1,170	1,347	61	47	925	956
New Orleans.....	2,286	3,217	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	1,980	1,464
New York.....	24,932	26,621	4,579	3,659	5,716	5,098	13,715	16,373	628	692	13,834	11,513
Oakland.....	1,864	1,475	189	168	451	361	1,158	887	44	36	1,519	953
Ola. City.....	2,079	2,312	267	361	534	723	629	764	52	28	1,177	792
Omaha.....	603	999	68	107	272	242	226	598	28	41	487	668
Philadelphia.....	9,690	5,259	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	1,003	(*)
Pittsburgh.....	(*)	8,748	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	235
Portland.....	931	713	266	143	59	45	589	493	17	33	1,153	593
Providence.....	471	532	66	30	52	37	302	420	9	14	159	165
Rochester.....	275	317	47	48	16	4	204	254	8	11	296	225
St. Louis.....	6,330	4,331	859	536	2,029	1,292	3,233	2,335	199	132	2,357	1,092
St. Paul.....	286	498	32	54	42	76	186	335	14	18	290	203
San Antonio.....	(*)	1,861	(*)	135	(*)	484	(*)	1,167	(*)	59	(*)	1,026
San Diego.....	1,118	1,200	135	102	306	412	577	658	35	27	1,006	677
San Francisco.....	2,969	3,355	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	2,227	2,770
Seattle.....	1,373	1,408	206	175	247	223	838	902	24	24	1,762	1,494
Syracuse.....	921	936	24	19	28	3	846	893	23	21	348	216
Toledo.....	904	798	129	103	151	139	591	515	33	35	126	160
Wash., D. C.....	8,261	(*)	1,070	(*)	1,968	(*)	4,867	(*)	130	(*)	4,234	(*)
Actual total‡	159,228	174,256	19,995	18,393	37,039	31,939	74,166	78,946	3,201	3,422	83,334	70,835

\* Data not available.

\*\* Includes "not stated".

† Based on cities reporting in both fiscal periods.

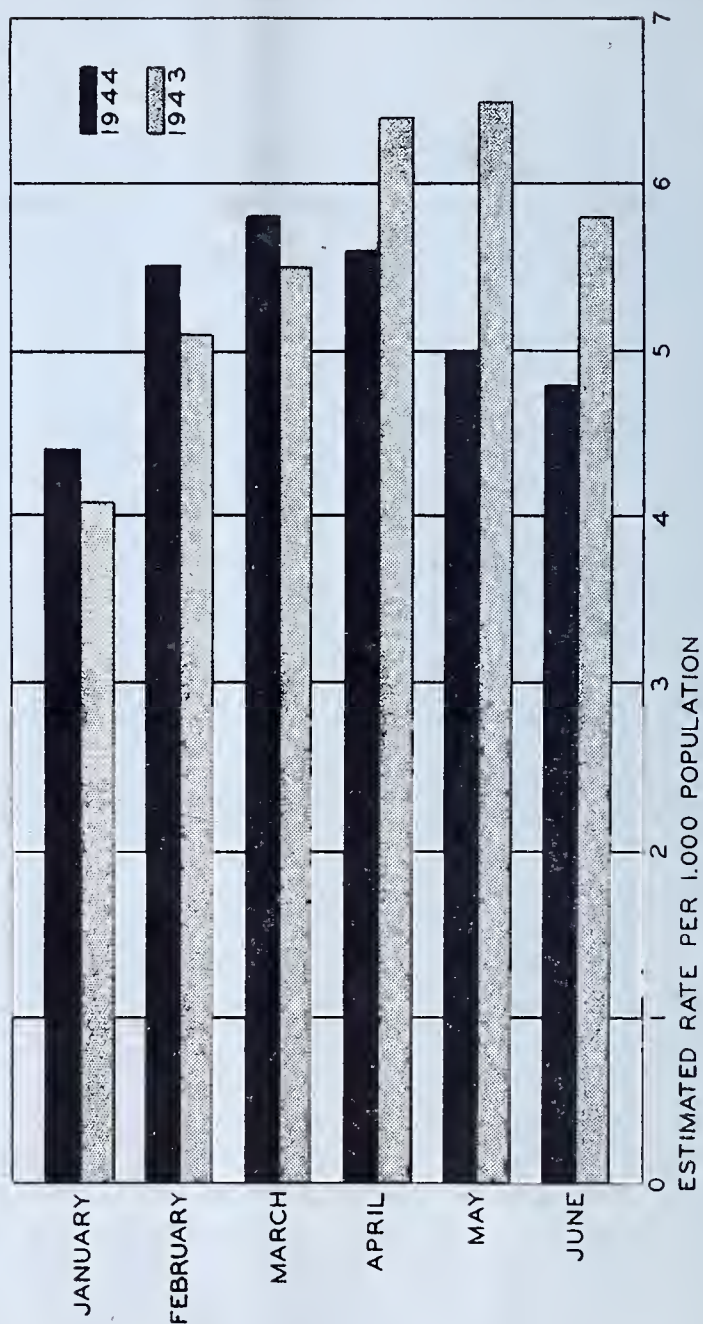
‡ Includes all reported cases.

¹ Based on 40 cities.

² Based on 37 cities.

³ Based on 39 cities.

ANNUAL SYPHILIS CASE RATES  
IN CITIES OF 200,000 POPULATION AND OVER  
BASED ON PROVISIONAL MONTHLY DATA  
1944 AND 1943





# Venereal Disease Information

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FEDERAL SECURITY AGENCY  
UNITED STATES PUBLIC HEALTH SERVICE

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# United States Public Health Service Evaluation of Massive Arsenotherapy for Syphilis: Cooperating Clinics of New York and Midwestern Groups

Since the first experiments with massive arsenotherapy for syphilis using neoarsphenamine by slow intravenous drip, many methods of intensive treatment have been developed. The present study is concerned with a group of 4,351 intensive treatments in which early syphilis contributed to the United States Public Health Service field study of massive arsenotherapy by the 22 cooperating clinics listed in table 1. This group of patients is limited to cases in the first 5 years of infection with or without active manifestations, treated during the period 1933-1943, inclusive. However, the analysis of results deals only with cases having positive evidence of primary or secondary syphilis.

Six different schemes were employed in analyzing the cases studied, as shown in table 2. (1) Slow intravenous drip with arsphenamine consisted of 800 to 900 mg. of neoarsphenamine in 2,000 to 3,000 cc. of saline or sugar solution administered over a period of 8 to 10 hours daily for 5 days, the total dose being 4,000 to 4,500 mg. (2) Slow intravenous drip with mapharsen usually consisted of 240 mg. of mapharsen in 2,000 cc. of solution administered in 8 to 10 hours daily for 5 days, the total dose being 1,200 mg. (3) Rapid intravenous drip with mapharsen usually consisted of 180 mg. of mapharsen in 1,000 cc. of solution administered in about 1 hour daily for 5 days, the total dose being 900

mg. (4) Multiple injection with mapharsen consisted of two syringe injections with 60 to 100 mg. of mapharsen daily for 5 to 10 days, the total dose being 600 to 1,000 mg. (5) Multiple injections with mapharsen and vaccine consisted of two syringe injections of mapharsen, each 60 to 70 mg., alternating with intravenous typhoid vaccine, the total dose being 600 to 900 mg. of mapharsen and 2 to 4 days of fever over a period of approximately 10 days. (6) Multiple injections with arsphenamine consisted of four syringe injections, each 75 to 150 mg. of arsphenamine, daily for 6 days, the total dose being about 3,000 mg.

In analyzing the results of treatment for syphilis, as for any disease of long duration, the chief difficulty lies in the fact that all cases undergoing a given course of therapy do not return for observation, so that the results of the treatment cannot be absolutely known for each case. For example, in the present group, 18 percent were not seen subsequent to discharge from the hospital, 67 percent were not seen more than one year after treatment, and 85 percent were not followed beyond the second year (table 3)\*.

There are various possible approaches to this problem, none of which are entirely accurate, but several of which should be avoided, because the error is known to be too great. In the first place, it can be seen from table 3 that any method which relates the total number of infectious relapses observed to the total number of patients treated gravely underestimates the real relapse rate. Many cases are lost immediately after treatment, yet only half of the infectious relapses observed occurred in the first 6 months. In fact 12 percent occurred after the first year following treatment.

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David C. Elliott, Surgeon, U. S. Public Health Service, was responsible for the promotion, organization and carrying through of this cooperative endeavor, reporting in *The Journal of the American Medical Association*, 117: 1160-1164, Oct. 4, 1941, the early progress on results of massive arsenotherapy for syphilis for the Midwestern and New York Groups.

\*A considerable part of the cases was treated in 1942 and 1943; therefore could not have been observed as long as 2 years.

TABLE 1.—*Hospitals cooperating in the U. S. P. H. S. field study of massive arsenotherapy for syphilis, and the number of cases of early syphilis contributed to the study by each*

Name and location of hospital	Cases of early syphilis treated
Bellevue Hospital, New York, N. Y. ....	1,054
Broadlawns Hospital, Des Moines, Iowa.....	91
Cleveland City Hospital, Cleveland, Ohio.....	10
Coles County Free Treatment Center, Mattoon, Ill.....	5
Cook County Hospital, Chicago, Ill.....	463
East Side Health District, East St. Louis, Ill.....	2
Henry Ford Hospital, Detroit, Mich.....	20
Herman Kiefer Hospital, Detroit, Mich.....	417
Indianapolis City Hospital, Indianapolis, Ind.....	560
Isolation Hospital, St. Louis, Mo.....	431
Long Island College Hospital, Brooklyn, N. Y.....	57
Louisville General Hospital, Louisville, Ky.....	134
Mt. Sinai Hospital, New York, N. Y.....	402
New Haven Hospital, New Haven, Conn.....	13
Presbyterian Hospital, New York, N. Y.....	258
Riker's Island Prison Hospital, New York, N. Y.....	25
St. Elizabeth's Hospital, Belleville, Ill.....	26
St. Joseph's Hospital, Bloomington, Ill.....	2
Sing Sing Prison Hospital, Ossining, N. Y.....	36
State General Hospital, Madison, Wis.....	12
University Hospital, Ann Arbor, Mich.....	297
University of Minnesota Hospital, Minneapolis, Minn.....	36
Total cases treated.....	4,351

Nor is it acceptable, where a portion of the cases has been followed for a considerable length of time, to calculate the percentage of "cured" cases using that portion followed as a base. This overestimates the satisfactory results obtained, since the chances are that the cases suffering an unsatisfactory outcome have been returned to treatment at some prior date.

A better procedure would be to use the number of patients still under observation at any given period as a base for computing a failure rate for that period, and then to combine these failure rates by means of a modified life-table technic in order to compute the total failure rate reached at the end of any given period of time. This method is satisfactory, under ordinary conditions

of follow-up, for a period of about 1 year after treatment. Beyond that time, however, so many patients will have been lost that a single clinical relapse will have a disproportionate effect on the cumulative failure rate. In the present material the percentage of the relapses which occurred more than 1 year after treatment (table 3) was about double the estimated total failure rate. Furthermore, there is implicit in this method of analysis the hidden assumption that the cases which are going to experience satisfactory results and those which are going to experience unsatisfactory results last from observation at the same rate. This assumption can be avoided if the status at last observation of each patient lapses before reaching any sort of final result.

TABLE 2.—*Methods of treatment evaluated in the U. S. P. H. S. field study of massive arsenotherapy for syphilis, number of cases of early syphilis treated by each method, and number of cases followed after treatment by each method*

Method of treatment	Cases of early syphilis treated	Cases followed after treatment
(1) Slow intravenous drip, neoarsphenamine.....	110	100
(2) Slow intravenous drip, mapharsen.....	2,451	1,971
(3) Rapid intravenous drip, mapharsen.....	450	398
(4) Multiple syringe injections, mapharsen.....	275	228
(5) Multiple syringe injections, mapharsen plus typhoid vaccine.....	779	637
(6) Multiple syringe injections, arsphenamine.....	263	241
Miscellaneous other methods.....	23	—
Total .....	4,351	3,575



TABLE 3.—Length of time cases were followed after treatment and the time at which clinical relapse occurred

Months after treatment	Cases treated	Clinical relapses	
	Percent still under observation	Percent occurring in period	Cumulative percent
1 .....	82.4	1.3	1.3
2 .....	76.7	3.3	4.6
3 .....	70.2	10.2	14.8
4 .....	64.6	13.0	27.8
5 .....	59.9	11.4	39.2
6 .....	55.2	12.3	51.5
7 .....	50.2	11.8	63.3
8 .....	46.1	8.9	72.2
9 .....	42.5	5.0	77.2
10 .....	39.1	5.1	82.3
11 .....	35.9	2.9	85.2
12 .....	33.3	3.0	88.2
15 .....	30.7	3.4	91.6
18 .....	24.4	3.8	95.4
21 .....	19.5	0.8	96.2
24 .....	15.5	2.1	98.3
30 .....	12.1	0.9	99.2
36 .....	7.4	0.4	99.6
and over.	4.0	0.4	100.0

ten into consideration. That is to say, at the probable outcomes for a group of patients lapsing while their blood tests are all positive at the end of, for instance, 3 months, should be estimated by means of those patients with known outcomes whose blood was also still positive at the end of 3 months. These considerations led to the method of analysis described in the following paragraphs.

The cases followed for any period of time are first divided into two groups, those reaching what might be considered a "final outcome" and those whose status when last seen could not be determined. Four broad groups were defined as final outcomes. (1)

A case negative for at least 3 months when last seen was considered to have experienced a "satisfactory" result. (2) A case still positive or fluctuating when last seen a year or more after treatment was considered to be "serologically fast." (A fluctuating case was defined to be one in which the serologic test on the blood had been negative at some time after treatment, but never for as long as 3 consecutive months, and had subsequently become positive. The last observation might be either positive or negative.) (3) A case positive or fluctuating at last observation which had previously fulfilled the criteria for satisfactory result was considered to be a "serologic relapse." (4) A case experiencing relapsing secondary syphilis was considered to be a "clinical relapse." Insofar as possible, reinfections were excluded from this last category by means of the following criteria: completion of the prescribed course of treatment; blood negative to all serologic tests on two consecutive observations at least 1 month apart following completion of treatment; new lesion, not typical of recurrence, appearing prior to a serologic relapse. Spinal fluid test results could not be used in defining the final results as listed, because of the fact that, for several of the treatment methods, such examinations were reported for too small a proportion of the cases.

On the basis of the serologic status at given observation periods after the treatment of those cases that experienced a final result, the probable final outcome of lapsing patients was calculated. For example, the

TABLE 4.—Results obtained with massive arsenotherapy in early syphilis, showing the estimated percent of cases in each final outcome following each method of treatment, by diagnosis at time of treatment

Method of treatment	Satisfactory		Serologically fast		Serologic relapse		Clinical relapse	
	Primary	Secondary	Primary	Secondary	Primary	Secondary	Primary	Secondary
low drip, neoarsphenamine.....	89.5	85.7	5.3	2.4	—	2.4	5.3	9.5
low drip, mapharsen.....	85.7	71.8	4.5	10.6	3.2	3.4	6.6	14.2
rapid drip, mapharsen.....	85.4	64.5	5.7	9.9	4.7	9.9	4.2	15.7
multiple injection, mapharsen.....	85.4	72.3	2.4	9.2	—	4.0	12.2	14.5
multiple injection, mapharsen plus typhoid vaccine.....	88.5	70.2	2.3	17.7	4.6	4.4	4.6	7.7
multiple injection, arsphenamine..	78.6	56.7	3.9	14.2	5.8	8.7	11.7	20.4
Total.....	85.7	70.4	4.3	11.9	3.5	4.6	6.4	13.1

cases in each final outcome were tabulated by serologic status 1 month after treatment. Then those cases that were last seen in the first month after treatment were tabulated by status at last observation. In each serologic status of the known cases, the proportion of satisfactory results, serologically fast cases, serologic relapses and clinical relapses was calculated. These proportions were applied to the unknown cases to find their probable results. This was done for all observation periods in which cases were seen for the last time without known final outcomes.

The tables of percentages presented in the text were computed from the combined known and estimated outcomes. However, in applying tests of significance, the number of cases with known outcomes was used as a base.

For each treatment method included in the study a greater percentage of satisfactory results was obtained among primary cases than among secondary cases. The percentages are given in table 4. Likewise, among patients with secondary syphilis, there developed more serologically fast cases, serologic relapses and clinical relapses proportionally than among primary cases. An average of 85.7 percent satisfactory results was obtained in primary syphilis as opposed to 70.4 in secondary syphilis. Six and four tenths percent of the primary cases suffered clinical relapse and 13.1 percent of the secondary cases. These differences are too large to be ascribed to chance.

In comparing the several methods of treatment, differences in the percentage of satisfactory results obtained do not appear large, especially with reference to cases of primary syphilis, but on analysis it was found that they cannot all be ascribed to chance. Neoarsphenamine by slow intravenous drip brought about the highest proportion of satisfactory results among both primary and secondary syphilis cases. This method, however, was discontinued by its originators because of its high reactivity. The treatment with the next highest percentage of satisfactory results, at least among primary cases, was mapharsen by multiple syringe injections combined with typhoid vaccine; among secondary cases

this method achieved about the same proportion of satisfactory results as followed by mapharsen by slow intravenous drip and mapharsen by multiple syringe injections without typhoid vaccine. The lowest percentage of satisfactory results, both with primary and secondary syphilis, followed the use of arsphenamine by multiple syringe injections.

With regard to the percentage of clinical relapses, no significant differences could be demonstrated between one type of treatment and another among primary cases. This may be due to the fact that the number of relapses was relatively small, particularly since the same differences were observed among secondary cases and the latter were significant. Rapid drip with mapharsen and multiple injections of mapharsen with vaccine gave the lowest percentages of relapses, while multiple injections of mapharsen without vaccine and multiple injections of arsphenamine gave the highest proportions.

Multiple injections of mapharsen with vaccine showed a lower clinical relapse rate than any other method of treatment, the difference being highly significant when comparison was made against rapid drip with mapharsen, slow drip with mapharsen or multiple injections of arsphenamine. The difference between this type of treatment and multiple injections of mapharsen without vaccine showed borderline significance. As in the analysis of satisfactory results the worst results obtained were with multiple injections of arsphenamine.

From the above analysis of results, it can be seen that although the differences between one treatment and another are not great, nevertheless all of them cannot be ascribed to chance. In general, excluding the original slow drip with neoarsphenamine which was found to be too reactive, the best results were obtained through the use of multiple injections of mapharsen combined with typhoid vaccine. Least effective, both in inducing satisfactory results and in preventing clinical relapse was multiple injections of arsphenamine. However, when the material was analyzed by amount of arsenical given (table 7) there were indications that the poor re-



TABLE 5.—Results obtained with massive arsenotherapy in early syphilis, showing the estimated percentage of cases in each final outcome following initial treatment and following retreatment

Stage at time of treatment	Satisfactory	Serologically fast	Serologic relapse	Clinical relapse
Primary syphilis.....	85.7	4.3	3.5	6.4
Secondary syphilis.....	70.4	11.9	4.6	13.1
Clinical relapse following routine treatment.....	59.2	29.5	6.8	4.5
Clinical relapse following massive arsenotherapy.....	68.9	17.2	4.0	9.9
Clinical relapses.....	67.2	20.0	4.6	8.2
Possible reinfections, any stage.....	73.5	17.0	3.8	5.7

Results obtained with this method may have been due to insufficient dosage. Among the remaining three methods there is little difference on the score of effectiveness in curing syphilis.

The therapeutic results, therefore, that might be expected from present methods of massive arsenotherapy are, at best, about 85 percent "cure" among cases starting treatment in the primary stage of the disease and 70 percent among cases starting treatment in the secondary stage. Primary cases have about 5 to 6 percent clinical relapse, and secondary cases from 10 to 13 percent. Perhaps as grave a consideration is the frequency of clinical relapses is the percent of primary cases and the 15 to 20 percent of secondary cases that either remain serologically positive or have serologic relapse, for any late manifestations of the disease which may occur will probably appear among these cases.

A small number of cases were followed after a second course of intensive treatment had been initiated, because of either a clinical relapse or a possible reinfection. A still smaller number were given a first course of

intensive treatment after experiencing a clinical relapse or becoming reinfected after routine treatment. In both groups the number of cases was too small to permit analysis for each method of treatment separately. The analysis of the results obtained in these cases, therefore, is made for all types of treatments combined.

No significant differences were found between the results obtained in original infections and those obtained in reinfections. And, as shown in table 5, while the reinfections showed both a larger percentage of satisfactory results and a smaller percentage of clinical relapses than did the relapses, the differences could not be demonstrated to be significant. This is probably due to the small number of reinfections. As might be expected, primary syphilis, first infection, gave much better results than did relapses. However, there was no difference in the results obtained among previously untreated secondary infections and those obtained among secondary manifestations occurring as a relapse after treatment, either routine or intensive in type.

Relapses occurring after routine treat-

TABLE 6.—Results obtained with massive arsenotherapy in early syphilis, showing the estimated percentage of cases in each final outcome following rapid and slow drip with mapharsen by quantitative Kahn test titer at time of treatment

Method of treatment	Satisfactory		Serologically fast		Serologic relapse		Clinical relapse	
	Titer 20 units or less	Titer over 20 units	Titer 20 units or less	Titer over 20 units	Titer 20 units or less	Titer over 20 units	Titer 20 units or less	Titer over 20 units
Rapid drip, mapharsen....	83.6	69.0	6.0	8.5	4.4	9.0	6.0	13.5
Slow drip, mapharsen....	80.2	72.1	4.4	12.0	7.2	3.3	8.2	12.6

TABLE 7.—Results obtained with massive arsenotherapy in early syphilis showing estimated percentage of cases in each final outcome for each method of treatment, by amount of arsenical given

Method of treatment	Amount of arsenical given	Satisfactory	Serologically fast	Serologic relapse	Clinical relapse
Slow drip, neoarsphenamine.....	Milligrams Less than 4,000 4,000 and over	87.4 88.0	6.3 4.8	— 1.2	6.3 6.3
Slow drip, mapharsen.....	Less than 1,200 1,200 and over	76.9 75.9	4.8 9.7	1.2 3.8	17.1 10.0
Rapid drip, mapharsen.....	Less than 800 800 and over	70.6 82.3	9.5 6.5	9.0 4.1	10.0 7.0
Multiple injection, mapharsen.....	Less than 1,200 1,200 and over	72.4 74.2	6.9 12.9	4.8 —	15.0 12.0
Multiple injection, mapharsen plus typhoid vaccine..	Less than 800 800 and over	72.0 83.0	14.8 10.0	3.6 —	7.0 7.0
Multiple injection, arsphenamine.....	Less than 2,400 2,400 and over	59.2 73.6	13.2 9.0	3.9 7.1	23.0 10.0

ment and relapses occurring after intensive treatment showed no differences in their response to treatment.

In comparing results of treatment started at different stages of syphilitic infection, it is pertinent to recall that the titer rises rapidly early in the disease. Therefore it might be expected that better results would be obtained in the treatment of cases with low titer. A considerable number of the cases treated by means of slow and rapid drip with mapharsen had blood specimens examined at the time of treatment by means of the Kahn quantitative test. With both these methods of treatment it was found that cases whose initial titer was 20 units or below had significantly more satisfactory results and fewer relapses than did cases with an initial titer higher than 20 units. These results are given in table 6.

It might naturally be expected that amount of arsenical administered would constitute an important factor in determining the outcome following various methods of treatment. In order to investigate this point the results following each method of treatment were analyzed at various dosage levels. Table 7 presents the final outcome for each treatment scheme above and below the dosage levels which gave the largest differences. It will be noted that the expectation concerning the effect of different amounts of arsenical is not entirely borne out. None of the differences are very great, and none are clearly significant. However, in nearly every case the differences are in the direction of better results with larger doses, and when treatments are combined, the difference is significant. In every instance more clinical

TABLE 8.—Results obtained with massive arsenotherapy in early syphilis showing estimated percentage of cases in each final outcome following administration of slow and rapid drip with mapharsen with and without bismuth

Method of treatment	Administration of bismuth	Final outcome			
		Satisfactory	Serologically fast	Serologic relapse	Clinical relapse
Rapid drip, mapharsen...	Bismuth given.....	92.4	3.8	3.8	—
	No bismuth given.....	70.4	8.4	8.4	12.8
Slow drip, mapharsen.....	Bismuth given.....	72.3	10.9	3.1	13.7
	No bismuth given.....	72.5	8.7	3.7	15.1



TABLE 9.—Results obtained with massive arsenotherapy in early syphilis, showing the estimated percentage of satisfactory results and of clinical relapses for each method of treatment, by age at time of treatment

Method of treatment	Percent satisfactory results		Percent clinical relapses	
	Under 25 years of age	25 years of age and over	Under 25 years of age	25 years of age and over
slow drip, neoarsphenamine.....	82.2	90.7	8.9	3.7
slow drip, mapharsen.....	73.3	81.3	14.5	8.2
slow drip, mapharsen.....	75.5	76.2	11.4	8.6
multiple injection, mapharsen.....	67.3	79.8	18.2	10.6
multiple injection, mapharsen plus typhoid vaccine.....	68.6	84.2	9.7	2.7
multiple injection, arsphenamine.....	58.4	74.1	23.0	9.5
Total.....	71.7	81.1	13.6	7.4

relapses occurred among the smaller dosage groups. The above trends are especially noticeable in the case of arsphenamine administered by multiple syringe injection.

In the evaluation of routine treatment, it has been found that the best results were obtained with schemes using both the arsenicals and the heavy metals.\* In the present series bismuth was administered in connection with the intensive treatment course in a portion of the cases given either rapid or slow drip with mapharsen. Table 10 shows the results following these two treatments divided according to whether or not bismuth was given. It can be seen that with rapid drip, the use of bismuth im-

proved the results markedly. Among the cases receiving this drug, there were 92.4 percent satisfactory results, compared with 70.4 percent among those not receiving it. Conversely, there were 12.8 percent of clinical relapses among those not given bismuth and none among those who did get it. Both these differences have high statistical significance.

Among the cases treated by slow drip, the results were not so clear-cut. When all cases treated by this method were divided only according to whether or not bismuth was given, no significant differences were found. It was noted, however, that bismuth was used more frequently in the treatment of secondary syphilis than in primary syphilis, and also that among primary cases it was given more frequently to the seropositives than to the seronegatives. When these groups were analyzed

Stokes, J. H.; Cole, H. N.; Moore, J. E. and others: Cooperative clinical studies in the treatment of syphilis. Ven. Dis. Inform., 13: 293, 1932.

TABLE 10.—Results obtained with massive arsenotherapy in early syphilis showing the estimated percentage of satisfactory results following each method of treatment, by race and sex

Method of treatment	Race		Sex		Race and Sex			
					White		Nonwhite	
	White	Non-white	Males	Females	Males	Females	Males	Females
slow drip, neoarsphenamine.....	91.1	80.6	87.9	—	91.1	—	80.6	—
slow drip, mapharsen.....	82.2	70.8	80.7	70.5	88.2	74.7	74.2	66.4
slow drip, mapharsen.....	77.9	74.6	83.8	66.5	86.4	66.7	82.6	66.5
multiple injections, mapharsen.....	78.7	70.0	77.2	69.0	77.7	80.7	76.6	62.5
multiple injections, mapharsen plus typhoid vaccine.....	84.5	67.5	80.3	64.8	90.1	74.2	73.6	61.0
multiple injections, arsphenamine..	68.2	63.1	64.9	—	68.2	—	63.1	—
Total.....	82.1	70.4	80.1	68.5	86.0	74.5	74.6	64.6

TABLE 11.—*Results obtained with massive arsenotherapy in early syphilis showing the estimated percentage of clinical relapses following each method of treatment, by race and sex*

Method of treatment	Race		Sex		Race and Sex			
					White		Nonwhite	
	White	Non-white	Males	Fe-males	Males	Fe-males	Males	Fe-males
Slow drip, neoarsphenamine.....	1.5	19.4	7.1	—	1.5	—	19.4	—
Slow drip, mapharsen.....	7.9	15.5	11.5	12.3	5.6	10.7	16.7	13.9
Rapid drip, mapharsen.....	15.4	8.1	7.1	13.4	10.2	22.2	5.8	10.4
Multiple injections, mapharsen....	11.7	15.8	15.7	11.5	15.9	3.2	15.6	16.1
Multiple injections, mapharsen....								
plus typhoid vaccine.....	3.7	8.9	7.1	7.0	5.0	1.5	8.6	9.2
Multiple injections, arsphenamine..	15.9	17.4	16.9	—	15.9	—	17.4	—
Total.....	8.1	13.0	10.5	11.3	7.1	10.0	13.6	12.1

separately, there still were no significant differences, although there was some indication that the use of bismuth tended to reduce the frequency of clinical relapses among both primary and secondary cases and to produce more satisfactory outcomes among secondary cases.

Differences in response to syphilotherapy may be inherent in certain characteristics of the patient population, even though these characteristics are not in any way determined by the disease or its treatment. In seeking to investigate these points the results of intensive therapy were analyzed by race, sex and age.

With regard to age a very definite bias was found in that with each of the six methods of treatment under consideration, patients under 25 years of age achieved fewer satisfactory results and met with more clinical relapses than did patients aged 25 years or over. The differences shown in table 9 are highly significant statistically. Of the older group 81.1 percent reached a satisfactory outcome as opposed to 71.7 percent of the younger patients, whereas only 7.4 percent of the older patients experienced clinical relapses compared with 13.6 percent of the younger ones.

From table 10 it can be seen that there are both race and sex differences in the response to rapid treatment for syphilis. The percentage of satisfactory results obtained was consistently higher for the white race than for the nonwhite races and was

also higher for males than for females. These differences remain significantly greater when the four race-sex groups are considered separately. There exist significant differences between the following pairs: White males show a greater percentage of satisfactory results than nonwhite males; white females than nonwhite females; white males than white females; nonwhite males than nonwhite females. All differences observed between the above pairs were in the same direction for all schemes of treatment with one exception; white females treated with multiple injection of mapharsen with vaccine showed a slightly higher percentage of satisfactory results than did white males. This difference is not significant.

The pattern of differences between the races and sexes is not so clear-cut when considering the proportion of clinical relapses as it is in the case of satisfactory results. The racial difference is still apparent, but there seems to be no difference between males and females. The clinical relapse rates are shown for race and sex in table 11. The nonwhite races show a significantly greater predisposition toward infectious relapse than does the white race for all treatments combined. Between the sexes, however, there is neither uniformity of direction in the differences from one treatment method to another nor is there a significant difference when all treatments are combined. The significant difference between the races is still apparent when



the sexes are considered separately. In only one treatment did the white race, both male and female, show a higher infectious relapse rate than the nonwhites. This was in the groups treated with rapid drip with mapharsen, and the difference is not significant in either sex. For both males and females the difference in the infectious relapse rate between whites and nonwhites is significant for all types of treatment combined.

The outstanding conclusion to be drawn from the foregoing analysis by patient population characteristics is that the group most resistant to treatment is that of young nonwhite females.

The present study is primarily concerned with the therapeutic efficacy of massive arsenotherapy; the detailed analysis of reactions is not yet complete. The only data concerning treatment complications yet compiled are derived from a hand tabulation of the abstracts available on Aug. 1, 1943. At that time a search was made for cases showing evidence of encephalopathy which advanced to the point of convulsions. It was found that for all types of treatment combined there were 3.2 fatal encephalopathic reactions per 1,000 courses of treatment and 3.9 nonfatal, a total of 7.1 per 1,000. No statistically significant differences could be demonstrated between individual clinics, methods of treatment, sexes or age groups. It was noted, however, that encephalopathy occurred more than twice as frequently among white persons as among nonwhites, and also that this type of reaction appeared to be more frequently fatal among white females than among white males or among nonwhites of either sex.

#### SUMMARY

1. The therapeutic results in a group of 4,351 massive arsenical treatments for syphilis have been studied.

2. It was found that the best results (excluding the highly reactive slow intravenous drip administration of neoarsphenamine) followed the use of multiple syringe injections of mapharsen combined with typhoid vaccine.

3. The most effective massive arsenotherapy yields 85 to 90 percent of satisfactory results in primary syphilis and 70 percent in secondary syphilis.

4. About 5 to 6 percent of the primary cases relapsed and 10 to 13 percent of the secondary cases.

5. Results following retreatment of patients relapsing after either routine or intensive treatment were about the same as those following the first treatment of patients with secondary manifestations.

6. Patients treated when the titer of the Kahn quantitative test on the blood was 20 units or below experienced more frequent satisfactory results and fewer clinical relapses than did patients with a titer greater than 20 units.

7. Results were slightly better among patients receiving larger doses of arsenicals than among those receiving smaller doses.

8. The administration of bismuth during the period of treatment appeared to improve the results obtained.

9. The following differences in response to treatment were noted: Patients over 25 years of age responded better than those under 25; males responded better than females; whites responded better than nonwhites.

10. Least satisfactory results to treatment were obtained among young nonwhite females.

11. Acute encephalopathy was observed in 7.1 per 1,000 treatments. Of these, 3.2 per 1,000 were fatal and 3.9 per 1,000 were followed by recovery. No difference could be demonstrated between treatments with regard to the frequency of this type of reaction.

# A Preliminary Report of Blood Testing, as Required by Alabama Law, in the First Three Counties Surveyed

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In July 1943 the Legislature of Alabama passed a unique law requiring all civilians between the ages of 14 and 50 years residing or living in the State of Alabama to have their blood examined for syphilis. The law resulted from the realization of the enormity of the venereal disease problem and the difficulty of control unless all infected individuals could be brought under treatment. In passing this law, Alabama became the first State in the Union requiring its residents to be blood tested for syphilis. The provisions of the law set forth that the testing be done "by a county basis" and that the sequence of counties be determined by the State Board of Health. The law also stipulates that all members of a family under 14 and over 50 years of age, living in the same household in which a positive reaction has been found, shall be blood tested.

In selecting the first few counties, consideration was given to the number of venereal disease clinics in operation and the readiness of the local medical profession to cooperate. It was felt that the blood testing program would be a failure unless the individuals who were found to be infected could be brought under treatment within a reasonable period after the survey. The procedure within a given county was, first of all, to determine the number of blood-test stations necessary to cover the county in such a way that no person would have to travel more than 2 miles to reach a station. After consulting local citizens as to the number of people living in a designated area, and by using O.P.A. registration figures and census fig-

ures, an estimate was made as to the expected number of people between the ages of 14 and 50 years that would attend each station. The basis for timing the stations was 40 people per hour for each person drawing blood.

After arranging for blood-test stations an intensive educational program was conducted for about 4 weeks. Syphilis as a subject was stressed, although there were references to the other venereal diseases. Where radio stations were available, this means of publicity was utilized. Addresses were made to all service clubs, women's clubs and all other groups that met in the county. Educational articles were carried in the newspapers, and the week before blood testing was to begin, the complete list of stations with the day, time and place of operation was printed in the local newspaper. Handbills signed by the local officials calling on the people to obey the law and showing the complete list of the stations were distributed. Posters announcing the time and location of the stations, quoting the law, and others giving venereal disease information were displayed over the county. Motion pictures were shown in schools, churches and in the open where buildings were not available. A portable electric generator made it possible to show pictures in any part of the county. Venereal disease pictures were shown in the local theaters. In each county, following the educational and preparatory work, a period of 2 weeks was allowed for the actual collection of specimens.

At each station there was one person (either a physician or a nurse) to collect blood and 4 clerks. All of the equipment necessary to complete the day's work was taken from the health department by each team every day. All needles and a few syringes were sterilized the day before

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and packed in covered, sterile catheter trays. Alcohol, cotton, tourniquets, wash-bans, numbered cards, laboratory forms and sterile test tubes completed the equipment carried by the teams. One car was used by each team to transport the workers from station to station.

Each person presenting himself at a blood-test station was given a prenumbered certificate card stating he had complied with the law. This card was filled in by the first clerk and passed to the second clerk; she in turn transferred the information to the laboratory form. The blood test certificate number was written by the clerk on this laboratory slip. The certificate card and laboratory slips were passed to the third clerk who then placed the number on the test tube. This tube was given to the patient who took it to the physician or nurse. After the tube was filled with blood, the patient returned to the third clerk who checked the number on the tube to see that it corresponded with that of the certificate and laboratory slips; he was then asked to sign his certificate and to keep it on his person. The fourth clerk was responsible for the cleaning and the care of needles and syringes.

The type of needle used for blood taking was 21 gage with a flange so that it could be attached to the test tube. Blood flowed by gravity when the tourniquet remained tied. The syringe and needle technic for drawing blood was used only when veins were so small that a 25 or 26 gage needle had to be used. Each evening when the team returned to the health department all needles were checked, washed, sterilized, and packed for re-use.

At the close of the day's operation, all blood specimens were brought into the health center, packed and expressed by bus or train to the central laboratory.

During the 2-week period when blood was actually being taken the most that the laboratory could do was to separate the serum from the clot, freeze and store it. After the survey, examination of the serums began.

A modified one-tube Kahn test, using standard Kahn test antigen, was applied to all original specimens. The results of

this examination were recorded as found, that is, either positive, doubtful, or negative. In all instances in which a positive or doubtful report was made on an original specimen, a second blood specimen was obtained and examined by the three-tube Kahn standard technic. The results of these tests were recorded also as positive, doubtful, or negative. These completed forms were sent to the Central Tabulating Unit for tabulation and alphabetical listing.

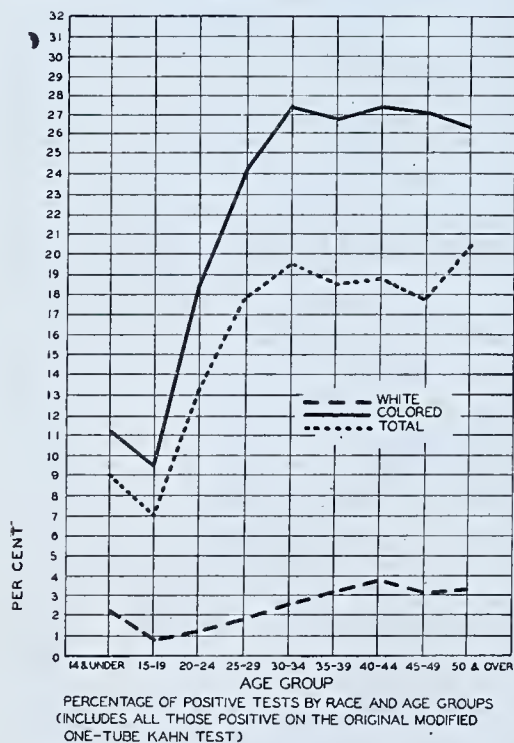
As lists were completed they were sent to the follow-up nurses to be checked against all venereal disease clinic rosters. All clinic patients found on the lists were given a new number, the number of their blood test certificate. Then these lists were checked against O. P. A. Book No. 3 records, by special permission from O. P. A. officials. The list compiled from O. P. A. records of individuals between the ages of 14 and 50 years who had not complied with the law was checked by many local people in the county, such as postmasters, principals of schools, teachers and superintendents of education, in order to determine whether these persons still resided in the county. A letter enclosing a copy of the blood test law was mailed to each person who had not complied with the law. Those who did not respond received a firmer letter. For those who did not respond to the second letter, a third letter was mailed to their employers asking for their cooperation. The sheriff was given the names of those who did not respond to the third letter.

All persons with positive, doubtful and unsatisfactory tests were notified by letter to appear at a specific clinic or at the health department. All persons with suspected syphilis, as shown by 2 positive or 3 doubtful reactions or a combination of these findings after more than 3 tests, were requested to present themselves to their own physician or to a clinic. An examination was made and if syphilis was diagnosed they were admitted and treatment was begun. All correspondence was done with plain paper and envelopes.

All clinic patients with early syphilis were treated by the 8-, 16- or 30-week plan (Eagle), and late latent by the 40-

week alternating course of bismuth and arsenicals.

The 3 counties in which the blood testing has been completed are Wilcox, Sumter and Lee. Wilcox and Sumter are counties in midwest Alabama, and Lee is a county in mideast Alabama. Wilcox and Sumter are rural counties with a Negro population of 78.3 percent and 79.4 percent, respectively. Lee County is also a rural country but is located in the heart of the cotton mill industry and has a Negro population of 56.6 percent. The normal estimated population of these counties is as follows: Wilcox, 23,770; Sumter, 23,135, and Lee, 32,970. However, using 60 percent as a rough figure to estimate the population in the age group concerned, the present normal estimated figures on population are inaccurate.



The figure shows the percentage of individuals positive on the original test by race and age groups. The percentage, beginning with the 15-19-year group in the white race, steadily rises until it reaches a peak in the 40-44-year age group. In the Negro the rate is frequently more than 10 times that in the corresponding white group. There is a steady rise among Ne-

groes to a maximum in the 30-34-year age group. In contrast to the white rate, this high rate is maintained.

Percentage of positive tests by race for 3 counties

County	White	Negro	Total
Wilcox	2.4	17.3	14.5
Sumter	3.6	24.96	20.8
Lee	1.8	19.4	11.2
Total	2.2	20.5	14.8

The table shows the percentage of positive blood reactors by race for each county. The highest rates are to be found in Sumter County but the 3 counties show more than 10 percent of the population between 14 and 50 years of age involved.

In Wilcox and Sumter counties follow-up investigations have progressed sufficiently to make certain additional statistical data available. In Wilcox County, of the 1,544 positive reactions found following a first serologic test, 127 (8.2 percent) proved by repeated tests not to be syphilitic; 185 have not been found as yet to be syphilitic; 13 have moved out of the jurisdiction, and 1,219 have been shown to probably have syphilis. Of these 1,219 cases, 638 were known to the health department, that is, they had been diagnosed as syphilitic and had received some treatment in the past, and 581 cases were unknown to the health department. Of the 581 cases, 545 have been brought under treatment and 13 have moved out of jurisdiction. The status of infection of these 545 cases was as follows: Early latent, 95; late latent, 436; cardiovascular, 2; late bone, 1; congenital, 11.

In Sumter County, where the follow-up work is still in progress, 2,252 were found to have a positive reaction to the first Kahn test. Of these, 197 (8.7 percent) were found not to be syphilitic, 588 have not yet been completely studied, and 1,367 were shown to probably have syphilis. Of the 1,367 patients, 663 were known to the health department and 704 were not. Of the 704 suspected cases of syphilis, 502 have received a diagnosis of syphilis and



have been admitted to treatment; 202 as yet have not been brought in for examination. Of the 502 cases admitted to treatment, the status of infection was as follows: Early latent, 104; late latent, 385; congenital, 13.

In Wilcox County, where the work is almost complete, there were obtained from D.P.A. records the names of 1,409 individuals, who apparently had not presented themselves for a blood test during the 2-week survey period. Some of these were duplicate names of individuals who had complied with the law. The group who had not complied with the law represented 13.2 percent of the individuals between the ages of 14 and 50 years. At the completion of the follow-up by correspondence, there were only 43 individuals, 1 white and 42 Negroes, who had not presented themselves for a blood test. After a lapse of time, this list was turned over to the sheriff. The 42 Negroes could not be found by the sheriff and presumably had left the county. The 1 white man as yet has not been prosecuted.

On the basis of present experience it appears that 80 to 90 percent of the population between the ages of 14 and 50 years will appear voluntarily for a blood test. It is, therefore, believed unlikely that law enforcement agencies will have to play any significant part in this program. In the first counties studied, over a thousand hitherto unrecognized cases have been detected and brought under treatment.

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## DIAGNOSIS

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Factors influencing false positive serologic reactions for syphilis due to smallpox vaccination (vaccinia). Grant O. Favorite. *Am. J. M. Sc., Philadelphia*, 208: 216-223, Aug. 1944.

Two groups, totaling 525 individuals, were studied regarding the incidence of biologic false positive serologic reactions for syphilis in persons recently vaccinated for smallpox. Out of 202 individuals on whom a single blood examination was

performed, 24 (11.8 percent) were found to be positive by one or more of the Kolmer simplified complement fixation tests, and the Kahn and the Mazzini flocculation tests. In the second group of 323 individuals who had smallpox vaccinations, the administration of typhoid vaccine and 2 injections of tetanus toxoid were studied to determine the role immunization played in the production of false positive reactions for syphilis. Three-fourths of these persons had been vaccinated 6 months previously, followed by a preliminary blood test, and then revaccinated. Kolmer, Kahn and Mazzini tests made 1 month later showed 15 persons with 21 positive serologic reactions. Of these, 5 occurred in the accelerated (vaccinoid type of reaction) group (71 persons), 4 in the primary (non-immune) group (6 persons), and 6 in the immune group (246 persons). The combined total of false positive reactions for the accelerated and primary individuals amounted to 11.7 percent, and the immune persons gave 2.4 percent weakly positive serologic reactions. To draw accurate conclusions as to the incidence of biologic false positive reactions for syphilis due to smallpox vaccination, one factor to be taken into consideration is the type of vaccination reaction. Evidence indicates that the immune response to smallpox vaccination can be disregarded as a significant cause of a false positive serologic reaction for syphilis.

The false positive serologic reactions for syphilis are transitory, appearing within 2 weeks of the date of vaccination and usually disappearing within 2 months (a few weakly positive reactions persisted as long as 4 months).

Typhoid and tetanus toxoid immunizations were found to have no significant bearing on the production of false positive serologic reactions for syphilis. Recently vaccinated individuals who gave a positive serologic reaction do not have a reactivation of their positive reactions following typhoid and tetanus immunizations 5 months later. Individuals with a false positive serologic reaction, when revaccinated for smallpox within 7 months, may again present a weak serologic false posi-

tive response for syphilis, even though the second vaccinia reaction is of the immune type.

Positive serums stored in the ice box at 4°C. for 7 months have a variable loss of titer, though not sufficient to be of differential diagnostic value.

#### **Multiple extragenital giant chancres.**

**Report of a case.** Walter F. Lever. *New England J. Med.*, Boston, **231**: 227-229, Aug. 10, 1944.

The case of a 28-year-old woman with 3 large deeply ulcerated crusted, extragenital chancres, 2 on the chin and 1 in the left inguinal region, seen at the Massachusetts General Hospital, is reported. Darkfield examination was positive for *Treponema pallidum*; reactions to the Hinton and Wassermann tests were also positive. Treatment was started with bismuth. On the day following the first injection a generalized macular skin eruption appeared. A diagnosis of secondary syphilis was made. The lesions were completely healed after 7 weeks' intensive treatment with mapharsen and bismuth subsalicylate in oil.

Lesions of the skin presenting the diagnostic triad (Stokes) of induration, slow course and satellite adenopathy, particularly if there is a profuse serous secretion and the margin of the ulcer eroded, should be regarded as a chancre until proved otherwise by repeated darkfield examinations of the lesion, as well as of the satellite lymph nodes, and by repeated serologic tests. All of these signs were present in the lesions of this patient.

Multiplicity of extragenital chancres does not occur in more than 2 percent of cases; especially rare is the presence of chancres at far-distant locations of the skin, as in this case.

**A discussion of the acute conditions arising in patients with lymphogranuloma venereum.** William P. Longmire, Jr. *Surgery, St. Louis*, **15**: 997-1016, June 1944.

The author presents a review of the case histories of 111 patients with lymphogranuloma venereum who have been ad-

mitted to the Johns Hopkins Hospital, with special reference to the acute conditions associated with this disease.

The Frei test was performed on 81 patients. In 74 it was positive, in 1 doubtful, and in 6 negative. There was adequate additional evidence in the 30 other cases to substantiate the diagnosis in spite of the absence of a Frei test or the presence of a negative result. Most of the patients had late manifestations of the disease.

Eight patients, with early infections, had severe constitutional reactions with elevations of temperature as high as 106° F. The anemia so frequently seen in patients with lymphogranuloma venereum is due to chronic loss of blood from the rectal lesions. Rectal hemorrhage severe enough to necessitate admission to the hospital occurred in 12 instances.

Twenty-three patients were treated for partial or complete intestinal obstruction. The tangential colostomy which was performed most frequently on the 20 patients requiring an artificial fecal outlet has proved unsatisfactory. A terminal transposition colostomy is now recommended.

Traumatization of infected tissue by biopsy, dilatation, proctoscopic examination, enema, or repeated digital rectal examinations may cause unfavorable reactions with elevations of temperature as high as 105° F. Traumatic perforation of the bowel occurred twice in this series.

Twenty-eight patients had 43 pregnancies during the course of an infection with the virus of lymphogranuloma venereum. One fetal death might be attributed to the presence of the infection. No maternal deaths were related to the disease. Lymphogranuloma venereum of the rectum is not necessarily a contraindication to normal vaginal delivery.

Signs and symptoms of an acute intra-abdominal lesion were present in 9 patients. The following lesions were found in 4 patients subjected to operation who had signs of an acute process in the right upper quadrant of the abdomen: (1) Multiple hepatic abscesses; (2) a nonspecific granulomatous lesion of the cecum with enlarged mesenteric lymph nodes; (3) sterile fibrinous peritonitis; (4) negative findings



With the exception of slight chronic cholelithiasis. Two other patients with clinical evidence of an acute intra-abdominal lesion were operated upon. One was found to have sterile peritonitis; the other had a chronic inflammatory mass of the cecum. Exploration was beneficial only in the second patient, who had a palpable abdominal mass before operation.

Perforation of an ulcerated area of the colon into the free peritoneal cavity occurred in 1 patient after a functioning ileostomy had been closed. Two other instances of perforation of an ulceration of the small intestine possibly due to lymphogranuloma venereum are described.

The frequency of the occurrence in these patients of acute arthritis and of certain inflammatory conditions of the eye is interesting regardless of the fact that there is as yet no definite evidence that such conditions are directly related to lymphogranuloma venereum.

**The complement-fixation reaction with the antigen of lymphogranuloma venereum (lygranum).** John E. Blair. J. Immunol., Baltimore, 49: 63-70, July 1944.

Complement fixation tests, using the method described by McKee, Rake and Shaffer with minor modifications, were made on 800 serums from 744 patients. The antigen used was lygranum C.F. and lygranum C.F. control. Of these, 157 were under treatment for syphilis, 4 had gonorrhea, 4 had lymphogranuloma venereum, and the remaining 579 were being treated for a variety of medical and surgical conditions. Of 153 cases of syphilis and 4 of gonorrhea, 42 (26.75 percent) gave 4-plus complement fixation reactions with lygranum in dilutions of 1 : 5 or higher. Frei tests were done on 17 of these patients and in 5 a reaction of 6 mm. or more in diameter was obtained. Thirty-six (22.92 percent) patients gave partial fixation reactions. Frei tests were done on 6 of these patients and were positive in 2. Four patients with lymphogranuloma venereum gave complete fixation reactions in dilutions up to 1 : 80 and partial fixation up to 1 : 320. Frei tests were positive.

A peculiar reaction was obtained in 4 patients with syphilis, in that 4-plus fixation occurred with the lygranum control as well as with the specific antigen in dilutions of 1 : 5 and 1 : 20. All gave negative Frei tests. Of the 579 patients with no history of exposure to venereal disease, 49 (8.46 percent) gave 4-plus complement fixation in dilutions of 1 : 5 or higher. Frei tests were done on 20 of these patients and were positive in 6. In 91 (15.71 percent) partial fixation reactions were obtained. No Frei tests were done. The remaining 439 (75.82 percent) gave negative cerebrospinal fluid reactions.

Of the patients whose serums gave complete fixation, about one-third gave positive Frei tests, giving reactions at least 6 mm. in diameter.

The significance of 4-plus fixations with serums from presumably non-exposed individuals is discussed. While some indicate lymphogranulomatous infection, some also appear to be due to other factors. The two possible interpretations of the significance of complement fixations with the antigen of lymphogranuloma venereum are (1) infection with the agent of lymphogranuloma venereum, either in an overt, clinically recognized form, or in a sub-clinical stage, and (2) cross-reactions with closely related viruses. Substantiation of the serologic test is obtained when the Frei test is also positive. A diagnostically significant fixation in the absence of a positive cutaneous test could suggest the existence of a hidden focus not readily recognizable in routine physical examination, and indicates a careful reexamination for further evidence of the infection, including the patient's history and possible contacts.

**A new technique in drawing blood for serodiagnostic tests. (Use of the hemospast.)** Kenneth E. Markuson. J. Indiana M. A., Indianapolis, 37: 400-402, Aug. 1944.

A new instrument, the hemospast, has been developed by John Soet.

The hemospast is a device for holding a standard 10 cc. rubber-stoppered vial and a standard double-pointed blood-letting needle. The stopper is composed of

self-sealing rubber so that a vacuum can be induced in the vial and maintained for an extended period. The simplest means of creating a vacuum is by the use of an ordinary water aspirator pump. A syringe needle is attached to the hose of the aspirator pump. The aspirating needle is inserted through the rubber stopper for a fraction of a second and then withdrawn. A vacuum of 20 to 30 inches is created in the vial. The average time for evacuating 50 vials is about 4 minutes. The vials so evacuated will retain sufficient vacuum for several weeks; therefore this process need not be repeated each time a blood specimen is desired.

The double-pointed blood-letting needle is inserted into the slot provided for it on the instrument and is fixed by a locking mechanism which allows proper alignment of the bevel of the needle. An evacuated vial is then placed into a sliding clamp which allows movement toward the fixed needle. After preparation of the patient's arm, the needle is introduced beneath the skin, but not far enough to puncture the vein. The vial is then pushed forward, allowing the back end of the needle to penetrate the stopper. This does not disturb the vacuum in the vial as the front bevel of the needle lies beneath the skin. The hemospast is now pushed slightly forward, allowing the needle to enter the vein. Entry into the vein is immediately detected by the flow of blood into the vial. When the vial is filled, the needle is withdrawn. Upon removal from the instrument, the vial is automatically sealed and is ready for labeling and mailing. The needle is removed from the instrument and placed in a disinfecting and cleaning solution. Another sterile vial and needle are inserted for the next extraction.

The instrument has been used on more than 7,000 patients during 1943. Physicians and technicians commend its speed, convenience, and simplicity; the reaction of patients has also been favorable.

**A viewing device for reading Kahn reactions.** Floyd Sell. *J. Lab. & Clin. Med.*, St. Louis, 29: 752-754, July 1944.

The author describes a viewing device

used at the Detroit Edison Company laboratories which permits the reading of Kahn results without removing the tube from the rack as well as the reading of individual tubes, when necessary.

The device is so constructed as to permit the transmission of light from a daylight fluorescent lamp in such a manner that any precipitate present in the test tube is illuminated and readily observed in contrast with the clear liquid in which the precipitate is suspended, with shields to exclude all extraneous light from the observer's eye. The standard Kahn rack is attached to a tilting lid, and easily adjusted. The device is enclosed in a 19.5 x 6 inch wooden box. The box operates with a lid which carries on its underside the holder of the standard Kahn rack. The lid can be fixed by means of a screw at an angle best suited to the reader. A 15-watt daylight fluorescent lamp with its auxiliary is attached to the bottom of the box. The underside of the lid is painted flat gray and the inside cavity of the box black, to provide a dark background. The bottom of the box is slightly curved to permit some motion of the box and corresponding motion of the fluid in the tube as it is observed for the presence of precipitates. A diagram of the viewing box is given. Reading instructions are also presented. All readings should be made in a darkened room.

**Repeated hemoptysis caused by aortic aneurysm: Three cases.** Eli R. Movit. *M. Bull. Vet. Admin.*, Washington, 21: 79-85, July 1944.

The author discusses repeated hemoptysis as a complication of aortic aneurysm and the failure to recognize an aneurysm as an underlying cause of pulmonary hemorrhage.

While the diagnosis of an aortic aneurysm was given in each of the three cases reviewed, in only one case was there a definite diagnosis of syphilis. At the first admission of the patient, a 52-year-old white man, in November 1942, there were strongly positive reactions of the blood and fluoroscopy showed a bulge which was definitely continuous with the aortic



shadow. After his discharge from the hospital in about 2 weeks he was given weekly injections of mapharsen. He was readmitted to the hospital in November 1943 having had several paroxysms of coughing followed by hemoptysis. His course in the hospital was uneventful until the tenth day when he had a massive hemorrhage and died in a few minutes. Autopsy showed the aorta, above the sinuses of Valsalva, to be uniformly dilated. In the descending portion, near the main stem left bronchus, there was an aneurysmal dilatation. This had ulcerated into the lung and communicated with a small bronchus.

**Syphilis and diabetes mellitus; a long-term clinical study.** Frank S. Perkin. *Ann. Int. Med.*, Lancaster, 21: 272-284, Aug. 1944.

By exhaustive investigation for the presence of latent as well as active syphilis, 54 (9.8 percent) possible cases of syphilis were found in the group of 550 diabetic patients seen at Receiving Hospital, Detroit, between 1928 and 1933. Race and sex seemed relatively unimportant. The diabetes in the syphilitic group tended to be unusually mild.

Nineteen cases of latent or tertiary syphilis were given prolonged syphilitic treatment under careful observation and, where possible, this was followed by glucose tolerance tests. In some cases no diabetic treatment, as diet or insulin, was prescribed. These cases were then observed for varying periods up to 12 years for changes in their diabetic status. Fourteen cases showed varying degrees of improvement in tolerance from moderate to a degree where apparently no diabetes was present. In 1 case no evidence of diabetes was present after 10 years.

The series suggests that there is some relationship between latent syphilis in the diabetic and the occurrence of gangrene. Syphilis should be suspected in the mild diabetic who develops gangrene, even in the presence of a negative serologic reaction. Careful histories and studies of the effect of antisiphilitic therapy may be necessary.

Even where the most marked improve-

ment was found, there was a tendency in later years for the diabetes to reappear. It is suggested that tertiary syphilis, as well as all other so-called causes of diabetes, is merely a precipitating factor in the potential diabetic.

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## TREATMENT

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**Penicillin treatment of early syphilis:**

II. J. F. Mahoney, R. C. Arnold, Burton L. Sterner, Ad Harris and M. R. Zwally. *J. A. M. A.*, Chicago, 126: 63-67, Sept. 9, 1944.

A series of approximately 100 patients have been treated in essentially the same manner as was employed in the group of 4 who were in the preliminary report (*Ven. Dis. Inform.*, 24: 355-357, Dec. 1943). Since the posttreatment period has been short for these patients, the conclusions are presented as informative only.

The therapy consisted of an intramuscular injection of 20,000 units of penicillin administered at 3-hour intervals, night and day, for 60 injections, the total amount of penicillin being 1,200,000 units. No other antisiphilitic medication was used. Herxheimer-like reactions of varying degrees of severity were observed during the first day of treatment in 86 patients. Because of the rapid disappearance of lesions, the main reliance in evaluating the therapy has been placed on the serologic tests.

On the basis of an arbitrary minimum of 75 days of satisfactory posttreatment observation, the records of 52 patients were available for scrutiny. The average observation period was 135 days. Of these 52 patients, 31 are considered as having responded in a favorable manner up to the present. In 7 patients there has been a progressive decline in the serologic titer and there is the possibility that these patients will be added to the favorably reacting group. Seven patients showed serologic relapse, and another 7 have serologic patterns which make their classification impossible.

From the study of these patients, the authors conclude that the contrast which is displayed in the groups of treated patients indicates that (1) very early infections respond in the most favorable manner and (2) the increase in probable failures in patients with secondary syphilis indicates the need of a more vigorous therapy than that used in this study. The evaluation of any therapy will require a prolonged trial, utilizing a wide variety of treatment schedules and a carefully controlled follow-up system.

**The treatment of early syphilis with penicillin: A preliminary report of 1,418 cases.** Joseph Earle Moore, J. F. Mahoney, Walter Schwartz, Thomas Sternberg and W. Barry Wood, Jr. J. A. M. A., Chicago, 126: 67-73, Sept. 9, 1944.

A Penicillin Panel, including the authors of this paper and later J. R. Heller, Jr., has been appointed by the Subcommittee on Venereal Diseases, National Research Council. Early syphilis is at present under investigation in 23 clinics or research centers which have agreed (1) to treat patients with early syphilis on assigned treatment schedules and (2) to pool their results under the Penicillin Panel. Only those patients in whom the diagnosis of early syphilis was indubitable, on the basis of actual demonstration of treponemes, were to be acceptable. It was decided that all cases were to be treated by the intramuscular route every 3 hours, day and night, to a total of 60 injections given in 7½ days, with totals of 60,000, 300,000, 600,000, or 1,200,000 units being given.

Through May 25, 1944, 1,587 case reports of early syphilis had been received, of which 1,418 were suitable for analysis. Only 113 of the entire number have been followed for 4 months or longer. From 663 cases treated with penicillin alone, organisms have promptly disappeared from open lesions within a range of 6 to 60 hours. There has been no observed instance of failure of lesions to heal, regardless of the single or total dose. There was apparent a trend toward serologic reversal

within a period of about 20 days after the start of treatment. The lowest incidence of relapse—and the most favorable serologic response—was in small groups of patients treated with 60,000 and 300,000 units, respectively, of penicillin plus known subcurative dose of mapharsen. The incidence of relapse, when penicillin is administered alone, is in direct relationship to the total dosage given by the intramuscular route in a 7½-day period, greatest with 60,000 units and least with 1,200,000. Relapse appears to be more frequent after intravenous than after intramuscular administration of comparable doses.

Penicillin was found to have a favorable effect in early asymptomatic neurosyphilis, acute syphilitic meningitis, early syphilis treatment resistant to arsenic and bismut, and infantile congenital syphilis. No opinion can as yet be given as to the effect of penicillin in the prevention of prenatal syphilis.

Herxheimer reactions were frequent but not serious and in no case interfered with subsequent treatment. Other reactions were negligible.

**Penicillin: Its usefulness, limitations in diffusion and detection, with analysis of 150 cases in which it was employed.** Wallace E. Herrell, Donald R. Nicholson and Dorothy H. Heilman. J. A. M. A., Chicago, 125: 1003-1011, Aug. 12, 1944.

Before the analysis of 150 cases in which penicillin was used, the authors discussed the methods of administration, the diffusion into various tissues, and suitable methods for determining the presence of penicillin in body fluids.

Sulfonamide resistant gonorrhea (1008): All of the 19 cases of sulfonamide resistant gonorrhea which have been treated by the authors by penicillin have given satisfactory results. The 2 patients who had gonorrheal arthritis in addition to the gonorrheal urethritis had striking symptomatic response to the arthritis, the arthritis being cured without instillation of penicillin into the joint. In 1 case in which the arthritis involved the interphalangeal joint of the thumb, there was



draining sinus and cultures revealed *Neisseria gonorrhoeae*. Roentgenograms revealed suppurative arthritis, with osteomyelitis. Without surgical intervention, complete healing resulted and roentgenograms after treatment were negative.

It is rarely necessary to use more than 100,000 to 150,000 units of penicillin as a total dose in the treatment of uncomplicated genitourinary neisserian infections.

**Experimental use of penicillin in treatment of sulfonamide-resistant gonorrhea.** Robert J. Murphy. Bull. U. S. Army M. Dept., Carlisle Barracks, No. 72: 101-105, Aug. 1944.

Of 306 patients with gonorrhea resistant to sulfanilamide therapy, treated with penicillin by one of several treatment schedules, 262 (88.8 percent) were cured following the first trial. All of the patients selected for this study had clinical signs of urethritis and a frank urethral discharge which gave positive spreads and cultures. Penicillin was administered intramuscularly in the upper-outer quadrant of the buttock. The observation period was 21 days. Daily inspection of the urethra for discharge and 2-glass urine tests were made in each case. There was only 1 reaction from penicillin treatment, a generalized urticaria.

The most effective dosage was 20,000 units of penicillin administered every 3 hours for 5 doses (a total of 100,000 units over a 12-hour period). Under this treatment scheme, only 1 failure resulted out of a total of 65 patients, and gonorrheal conjunctivitis, a complication in 3 cases, responded promptly.

Of the 34 failures retreated with 10,000 units of penicillin every hour for 10 doses (a total of 100,000 units over a 9-hour period), 3 did not respond. Retreatment was effective when the patients were given 10,000 units of penicillin every 3 hours for 16 doses (a total of 160,000 units over a 45-hour period).

The criteria of cure were negative spreads and cultures of the prostate fluid taken at 48-hour, and 7-, 14-, and 21-day intervals, and retreatment on another schedule when

persistent clinical findings were confirmed by positive laboratory evidence.

The foremost clinical observation in the series was the persistence of urethritis following treatment, although spreads and cultures remained negative. In the majority of cases the infection disappeared about 1 week following treatment.

In 4 cases of gonorrheal arthritis with concomitant gonorrheal urethritis other treatment procedures were required for the arthritis. Penicillin therapy was not effective in gonorrheal epididymitis which was a complication in 8 cases.

The 8 treatment schedules are outlined and the results are presented in a table.

**Syphilis and pulmonary tuberculosis in the Negro.** Reuben Hoffman and George G. Adams. Am. Rev. Tuberc., New York, 50: 85-95, Aug. 1944.

In an attempt to determine the effect of syphilis on tuberculosis, serologic tests for syphilis were performed upon 1,705 consecutive adult admissions to the Maryland Tuberculosis Sanatorium, Colored Branch, Henryton, Md. Of this group, 507 (29.7 percent) were found to have positive serologic reactions. Ten percent had early latent syphilis (less than 4 years' duration), 70 percent late latent (more than 4 years' duration), 15 percent involvement of the central nervous system with positive cerebrospinal fluid, and 5 percent cardiovascular involvement. In most of the cases there was a history of syphilitic infection prior to the onset of tuberculosis, and about 50 percent had received inadequate antisyphilitic treatment.

An analysis of the findings, based on the amount of pulmonary involvement and the predominant type of pulmonary lesion in the negative and positive serologic groups on admission, and the percentage of deaths occurring in both groups in relation to the admission classification of the tuberculosis (no treatment being given for the syphilis) showed no significant difference. The difference between the percentage of syphilis in the minimal and the far advanced tuberculosis groups was less than 7 percent and could not be used to infer that syphilis

lowered the resistance of a patient to tuberculosis.

The authors feel that their conclusions that there is no biologic relationship between the two diseases are justified from these findings.

Except in cases of pregnancy and in the presence of the infectious stages of syphilis, the determination of antisyphilitic treatment of the patient rests on the prognosis of the tuberculosis. If the prognosis for the tuberculous infection is good and the status of the syphilis justifies it, antisyphilitic treatment is instituted. Opinions differ as to whether the late latent syphilis in tuberculous patients should be treated. The general opinion based on clinical impressions is that the arsenical drugs activate tuberculous lesions.

The authors state that this study does not include the problem of false positive serologic reactions for syphilis in the presence of tuberculosis, the number of patients and the number of repeated examinations being too few. The study suggests, however, that with careful history taking and careful diagnostic procedures, frequently repeated when in doubt, the problem is not important.

#### **Insulin and electric therapy in general paresis.** Paul J. Tomlinson. *Psychiatric Quart.*, Utica, 18: 413-421, July 1944.

Eighteen cases of psychosis with syphilitic meningo-encephalitis were treated with insulin or electric therapy at the Gowanda State Homeopathic Hospital, Helmuth, N. Y. Of these, 13 received insulin, 3 electric shock, and 2 both insulin and electric shock. One had previously been treated with metrazol. All had had malarial therapy and tryparsamide with no improvement in the mental status.

The technic of insulin therapy, previously described by the author and coworkers, consisted of the administration of 15 units of insulin to the fasting patient at 6 a.m. The patient is given breakfast and additional fruit juice and sugar at 9 a.m. The dosage is increased by 5 units daily until the condition of the patient at the time of termination of the day's treatment is such that he is bordering on insulin coma.

When this stage is reached, the dosage held stationary for succeeding treatment. If, because of atmospheric conditions a change in the individual's insulin tolerance, he goes into coma before the 3-hour interval has elapsed, the treatment for that day is interrupted by 33⅓ percent glucose given intravenously. The dose is lowered by 5 to 10 units the next day. The average maximum dose of insulin in the author's series was 42 units, the range of individual patients being from 20 to 60 units. The duration of treatment ranged from 9 to 160 days, with an average of 54 days.

Electric shock therapy was given to 5 patients who received an average of 10 treatments each. Four were much improved by this therapy.

Rationale of the application of insulin and electric therapy to paresis is considered on a basis of psychotic reaction types. Seven cases of the group were considered as showing catatonic syndromes, 1 paranoid, 3 expansive manic, and 4 generalized deterioration. The catatonic and manic types showed a favorable response to either subcoma insulin or electric shock therapy. Of the 4 paranoid patients, only 1 showed improvement. The 4 patients with generalized deterioration showed no improvement in their mental status, 3 following insulin and 1 after electric shock; however, there was some improvement in the physical state of the patients.

None of the patients treated with electric shock showed any aggravation of the central nervous system syphilitic processes and no complications were noted.

Although the number of cases in this series is too small to make any definite evaluation of the relative merits of subcoma insulin and electric shock, the author believes that the favorable results seen in the manic expansive and catatonic cases justify the continued use of these therapies when indicated.

#### **Gonorrhoea in North Africa and the Central Mediterranean.** Douglas J. Campbell. *Brit. M. J.*, London, No. 4357: 44, July 8, 1944.

Since the invasion of the Latin coun-



ies, gonorrhea has proved intractable to the former accepted methods of treatment by chemotherapy. While the Army was in Algeria and Tunisia, the response to treatment was similar to that in the United Kingdom, although gonococcic arthritis was common. At first, sulfapyridine was administered as a course of 20 to 30 gm. in 5 days, and toward the end of the campaign sulfathiazole, 10 gm. in 2 days, was introduced. There were 70 to 75 percent satisfactory results.

When the campaigns in Sicily and Italy began, early treatment failed almost completely. The unsuccessful cases in the hospitals in North Africa had to be evacuated, and venereal disease treatment centers were opened in Sicily. Less than 25 percent of the patients were responding to the short courses of chemotherapy and of these many had relapses. Dosage was increased to 25 to 30 gm. of sulfathiazole or sulfapyridine in 4 to 5 days. Second courses were necessary in 70 to 80 percent of cases after 5 to 7 days' irrigation treatment. Large numbers of men reached the main venereal disease units with gonococcus-positive discharge after having received as much as 130 gm. of various sulfonamides. The economic conditions drove the women of Sicily and Italy to prostitution. As the campaign progressed north there was a slight improvement, but less than 50 percent of cases of acute gonorrhea responded to an initial course of 25 to 30 gm. of sulfathiazole and relapses were common. Resort to pyrexial therapy by means of intravenous T.A.B. vaccine during a second course of chemotherapy became a necessity. Some success followed the use of the standard Army gonococcic vaccine.

The author says that the Americans have found the same conditions among their troops and have had to use penicillin as alternative therapy. If similar difficulties are met throughout Europe, gonorrhea will be an immense scourge.

**Sulfonamide ointment in routine prophylaxis of chancroid disease.** Herman S. Zeve and Sol S. Schneierson. U. S.

Nav. M. Bull., Washington, 43: 391-392, Aug. 1944.

The authors, who are stationed in a tropical area, varied their method of routine prophylaxis by using a mixed ointment containing one-third 5 or 10 percent sulfanilamide or sulfathiazole ointment and two-thirds calomel ointment, instead of the calomel ointment alone, in the final phase of the prophylaxis routine. For a period of 9 months, 10,368 prophylactic treatments were given to nontransient personnel whose course was followed. Since the institution of this method of prophylaxis, only 2 cases of chancroid were seen. In one patient the prophylaxis was recorded 26 days before admission and he may have had subsequent exposures without prophylaxis, and in the other, treatment was recorded 2 days before admission whereas no prophylaxis was recorded for an admitted exposure 2 weeks previously. During this period there were 70 other admissions for chancroid. These men either had received no prophylaxis or had not received the sulfonamide-calomel routine.

From their observations, the authors advocate the addition of a sulfonamide ointment to the calomel ointment in the Navy venereal disease prophylaxis routine.

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## LABORATORY RESEARCH

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**A method for the recovery of penicillin from the urine.** Lawrence H. Sophian. J. Lab. & Clin. Med., St. Louis, 29: 769-771, July 1944.

The U. S. Marine Hospital, Staten Island, N. Y., has perfected a method for the recovery of penicillin from the urine of patients being treated with penicillin.

A large container is kept in the ice box for collection of urine from patients under treatment with penicillin. Collections may be made in this manner for 48 hours without loss of the drug. The urine is acidified with concentrated hydrochloric acid and brought to a pH of 2 as determined

by the color change produced with methyl violet indicator. Approximately 6 to 7 cc. of acid are needed for each liter of urine. Amyl acetate is added to the urine in a proportion of 1:3. A reservoir bottle with an outlet at the bottom is a convenient container for mixing. The mixing of the urine and acetate requires inverting the bottle 12 or 15 times (too much agitation causes foaming). The bottle is placed in the ice box for 4 hours to allow separation of the urine and acetate, then the urine is drawn off through the lower outlet leaving the penicillin dissolved in the amyl acetate. Any foamy middle layer is passed through several thicknesses of gauze to recover as much of the amyl acetate as possible.

The amyl acetate extract is placed in a 1-liter separatory funnel. Approximately 20 cc. phosphate buffer solution are added to it for each liter of amyl acetate. The buffer is prepared by mixing approximately 1 part sodium acid phosphate to 2 parts disodium phosphate by weight, adjusting to pH 7. After mixing the buffer solution with the amyl acetate, some color (the pigment which occurs along with penicillin) will be seen to transfer to the buffer solution. The buffer solution is adjusted to pH 6.5 by gradually adding 5 percent sodium carbonate solution or 2 normal sodium hydroxide solution. The pH is determined by testing of single drops of the solution with brom thymol blue indicator, agitating thoroughly after each addition. When pH 6.5 is reached, practically all the color will have passed from the amyl acetate solution into the buffered aqueous solution. The transfer of penicillin is almost quantitative. The separatory funnel is placed in the ice box for 6 hours to complete the separation and the amyl acetate is then drawn off. The amyl acetate may be used again.

Testing for activity of penicillin is done by the dilution method against staphylococcus H, as described by Hamre, Rake, and coworkers. A satisfactory product is then Seitz filtered into sterile vials. Useful concentrations of 3,000 units of penicillin or more per cubic centimeter may be obtained. An average yield of 30 percent

of the administered amount has been obtained, and the antibiotic and pharmacologic effects have been identical with those of commercial penicillin. For every one million units given the patient, 300,000 units can be recovered in a form suitable for re-use. So far no toxicity has been found.

The aqueous solution of the filtered extract is kept in an ice box in vials until used. The extract has been used in doses equivalent in amount to the commercial product in patients with gonorrheal urethritis with equal effectiveness and without reaction. Storage for 60 days at  $-10^{\circ}\text{C}$ . demonstrated complete maintenance of antibiotic activity.

**The acute toxicity for mice of "mapharsen" and sodium sulfathiazole administered separately and in combination.** Elizabeth M. Cranston, William G. Clark and Ernest A. Strakosch. *J. Pharmacol. & Exper. Therap.*, Baltimore, **81**: 284-287, July 1944.

Experimental studies were made on mapharsen and sodium sulfathiazole to determine whether they are synergistic, additive, antagonistic or without effect when used in combination or separately in the treatment of both syphilis and gonorrhea in the same patient. Sodium sulfathiazole in a 10 percent solution in distilled water and mapharsen in a 0.3 percent solution in distilled water were administered to young male and female mice of strain A weighing between 14 and 20 gm. Studies on the separate toxicity of the two drugs were run in parallel over a period of about 1 month and the combined toxicity experiments were conducted over a period of about 6 weeks in groups of 10 to 20 animals each. The results were summarized.

The  $\text{LD}_{50}$  of intraperitoneally administered mapharsen was found to be  $34.0 \pm 0.5$  mg. per kilogram and of sodium sulfathiazole administered similarly  $1.32 \pm 0.02$  gm. per kilogram. The combined toxicity of mapharsen and sodium sulfathiazole was found to be greater than the toxicity of either drug alone. Calculations of the data presented showed the  $\text{LD}_{50}$  of the



ombination to be 65 percent  $\pm$  1.5 percent of the LD<sub>50</sub> of each drug alone.

The toxicity of sodium sulfathiazole intraperitoneally reported by the authors is approximately the same as values reported by other investigators for subcutaneous injections, and somewhat lower than the results with intravenous injections. The toxicity of mapharsen intraperitoneally was found to be lower than that reported by others using subcutaneous as well as intravenous injections. Although the combination of both drugs was found to be more toxic than either alone (the LD<sub>50</sub> of the combination being 65 percent of the LD<sub>50</sub> of each alone), the combined toxicity was not synergistic since if that had been the case the LD<sub>50</sub> of the drugs together should have been less than 50 percent of the LD<sub>50</sub> of each alone. The results obtained indicate that the toxic effects are additive but are less than algebraic summation.

**Maintenance of moisture in bacteriologic culture media.** George H. Chapman. J. Lab. & Clin. Med., St. Louis, 29: 751, July 1944.

The author describes the method used by the Clinical Research Laboratory, New York, to maintain the moisture of stored bacteriologic culture media. Petri dishes with porcelain covers glazed on the outside are poured approximately 25 ml. each and are stored in an electric refrigerator. The average loss from evaporation, judged by loss of weight, is 0.10 ml. per day. The date each medium is poured is noted on a slip of paper and attached to the set of dishes. When a plate is needed sterile water is added, 0.10 ml. for each day since it was poured, and is spread lightly by a sterile glass spreader. The plate is allowed to stand about 30 minutes and is then inverted to drain off any unabsorbed moisture. It is then ready for use.

Different types of blood agar and media containing critical concentrations of bacteriostatic agents have been kept for considerable periods of time and have been found satisfactory, while other plates from the same lot but not so treated gave poor results.

**Studies on lymphogranuloma venereum:**

**II. The association of specific toxins with agents of the lymphogranuloma-psittacosis group.** Geoffrey Rake and Helen P. Jones. J. Exper. Med., Baltimore, 79: 463-485, May 1944.

From their study with inoculations into the chick embryo, the authors have found that toxins, which resemble in most respects bacterial endotoxins, are associated with the agents of lymphogranuloma venereum, meningo-pneumonitis, and mouse-pneumonitis as they grow in the yolk sac of the chick embryo. They are labile and are not readily separated from the bodies of the agent. They kill mice rapidly after intravenous, and in some cases after intraperitoneal, injection but the minimal lethal dose is relatively large and, in those freshly harvested yolk sacs which have been tested, has corresponded to about 36 million infective units. Characteristic lesions are produced in all mice except those which die very rapidly, and are found especially in the liver where necrosis of the midzone of the lobule occurs.

Antitoxic serums which are effective against a few lethal doses of the toxin can be produced in rabbits or chickens by using either toxin or toxoid as antigen. Such serums behave in a manner analogous to antitoxins against bacterial endotoxins and they do not neutralize by the law of multiple proportions. Antitoxic serums can also be obtained from human beings convalescent from at least one of these diseases. The toxins and antitoxins appear to be highly specific and they may offer a useful tool in distinguishing between different members of this closely interrelated group.

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## PUBLIC HEALTH ADMINISTRATION

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**The San Francisco Separate Women's Court.** Richard A. Koch. J. Social Hyg., New York, 30: 288-295, May 1944.

The San Francisco Separate Women's

Court was established in 1943 to provide an adequate and enlightened social facility which could be used as an intake center for women arrested for vagrancy, prostitution, disturbing the peace and related misdemeanors.

Where previously about half an hour was spent hearing these defendants in a group, this new facility provides a small court room, examination clinic, private interviewing rooms for social workers and office space, 16 separate rooms with 2 beds, a washbasin and lavatory in each room. The premises are supervised by police matrons but the maximum possible privacy exists. All women are given individual rooms if possible; careful segregation is the rule. To provide for the maximum degree of segregation during the observational quarantine period, all meals are served in the individual rooms.

If upon arrest of an individual enough evidence exists to hear the case, it is postponed 72 hours in order to provide for social diagnosis, interpretation, and determination of the presence of a venereal disease. If the evidence presented is insufficient, the patient is placed under observational quarantine and held under the quarantine authority of the San Francisco Department of Public Health. If found to be infected with a venereal disease, she is held under treatment quarantine until noninfectious, and if found guilty by the jurist, disposition of the case is based upon previous history of the defendant and mitigating or aggravating circumstances, and may be either a jail sentence or release to probation custody. Treatment of a venereal disease follows as a natural sequence.

The cost of establishing the court, including alteration, equipment and supplies, was approximately \$18,000. The yearly operation cost for salaries is \$88,000, and cost of food and maintenance is \$12,000, a total annual expenditure of \$100,000.

For the period Mar. 18, 1943 to Jan. 1, 1944, the Separate Women's Court dealt with 859 women, which resulted in 970 hearings. Disposition of these hearings resulted in 422 (44 percent) sentenced to

the county jail; 178 (18 percent) given suspended sentences with probation; 10 (10 percent) given suspended sentences under special conditions; 223 (23 percent) dismissed; 36 (4 percent) referred to the juvenile court, and 11 committed to the psychiatric ward of the county hospital or committed to a State mental hospital.

**Correspondence.** H. C. Moore. J. Missouri M. A., St. Louis, 41: 195, September 1944.

In a letter to the editor, the author, who is stationed with the Army Service Forces Seventh Service Command, states that for the first 2 months of 1944 the venereal disease rates in the Seventh Service Command area were 50 percent higher than those of the corresponding months of 1943 and enlists the aid of the medical profession in reducing the rate of venereal disease in the Army with the following suggestions:

- (1) Refuse to treat officers or enlisted personnel of the Army without approval of each soldier's commanding officer;
- (2) support community sentiment against prostitution and assume leadership in an adequate preventive medical program;
- (3) in treating civilians with venereal disease insist upon continuity of treatment to cure using the services of the health officer when necessary to insure this. A more cautious attitude on the part of the physician and improvements in the thoroughness of physical examination are indicated in the treatment of female patients with gonorrhea.

Observations on the inadequacy of present methods imply: (1) The medical absurdity inherent in the certificate of freedom from venereal disease and the dangers involved in the common practice of giving patients negative laboratory reports, (2) the responsibility which the physician must assume for attempting to control the sexual activities of patients while in the infectious stage of the disease, and (3) the need for participation of the private practitioner in an effort to "sell" modern venereal disease prophylaxis to the public.



ood tests for all soldiers leaving service. Georgia's Health, Hapeville, 24: 1, Aug. 1944.

With the cooperation of the Army, the S. Public Health Service, and the state and local health departments, blood tests are being performed on all men mustered out of the Army, and those with evidence of syphilis are referred to local health departments for follow-up treatment.

Additional separation centers are planned throughout the country. At present, Fort McPherson is the only one in operation in the Fourth Service Command, the serologic tests being handled by the Georgia State Health Department. Since Aug. 1, 1944, State laboratories have received approximately 1,200 specimens for testing.

An unsurpassed record. Bull. Dept. of Health of Kentucky, Louisville, 16: 258-259, July 1944.

Out of approximately 1,600 men of the 2220th Army Air Base Unit who received training over a 15-month period at Bowling Green there was not one case of venereal disease known to the officers.

Attributable factors were an intensive venereal disease educational program and operation of a full-time Army prophylactic station in Bowling Green, as well as control measures executed by the Warren County Health Department and other cooperating agencies.

Medical conservation of manpower in a shipyard. Robert L. Brown. J. M. A. Georgia, Atlanta, 38: 208-213, July 1944.

The Kahn test for syphilis is part of the preemployment examination at the Brunswick Shipyard of the J. A. Jones Construction Company, Inc. The yard medical department cooperates with the local board of health, and patients with positive reactions are advised to secure treatment either from the board of health or a private physician.

Out of a total of 12,784 persons examined, 52 per 1,000 (5.2 percent) had positive Kahn reactions. The number of

white applicants found to be positive for syphilis was 27 per 1,000 (2.7 percent), and among the Negroes, 200 per 1,000 (20.0 percent).

A survey of syphilis in first admissions to a mental hospital over a five-year period. R. W. Medlicott. New Zealand M. J., Wellington, 43: 93-96, Apr. 1944.

From 1939 to 1943, inclusive, of 1,342 first admissions to the Porirua Mental Hospital who were given blood Wassermann tests, 67 (5.06 percent) had positive reactions. The average age of these patients (47 men and 20 women) was 47 years.

Of the 67 cases, 52 were paretics or taboparetics, 3 were asymptomatic neurosyphilitics, and 12 showed no involvement of the central nervous system.

The author concludes that although the incidence of syphilis and paresis is relatively low for New Zealand, there is need for improvement in the control of these diseases. The public should be educated to the importance of early medical advice and there should be a more general use of the routine Wassermann examination. He cites the advances made by other countries.

The physician's attitude toward prostitution and juvenile delinquency. Abraham L. Wolbarst. Urol. & Cutan. Rev., St. Louis, 48: 220-223, May 1944.

Some years ago the author distributed a questionnaire among the members of the American Urological Association covering their views on the physiologic character of the sex urge and its moral aspects. The confusion of medical thinking on this subject was revealed by the fact that while 73 percent of those who replied considered sex indulgence by the unmarried a physiologic function and not a vice, 62 percent of the replies declared that indulgence is not essential to normal health and of these, 32 percent declared that it is the exercise of a physiologic function and not a vice. Also, while 69 percent considered prolonged abstinence by both sexes consistent with normal health, 57 percent believe that abstinent men and women are not the men-

tal and physical equal of those who are not abstinent.

This confusion in medical thought makes the solution of sex problems difficult. If doctors, who should understand sex and what it means to the individual and to the race, cannot agree on the fundamentals, it cannot be expected that laymen and theologians will have a rational understanding of the subject. Until medical men apply scientific processes objectively without the injection of their religious and moral aspirations, no improvement of the serious question in relation to delinquency and prostitution can be expected.

**A study of 280 patients in the venereal disease isolation hospitals of Puerto Rico.** *J. Social Hyg., New York, 30: 269-287, May 1944.*

A study was made of 280 women (244 prostitutes and 36 nonprostitutes) in the venereal disease isolation hospitals at Caguas and Troche, Puerto Rico. The study includes information in regard to age, race, civil status, religion, physical handicaps, medical diagnosis, sources of infection, social background, social problems, education, training, work history, vocational choices, sex history and circumstances, factors leading to prostitution, length of time in prostitution, influence of friends and facilitators, places of soliciting and sex contacts, types of customers, income, attitude of patient toward way of living, and worker's impression of rehabilitation possibilities.

Approximately 95 percent of the women were being treated for gonorrhea and 37 percent for syphilis. One-third of them were being treated for a combined infection of gonorrhea and another venereal disease, usually syphilis.

More girls were in the 18-year age group than any other single age group, and over half were under 21 years of age. Fifty-six percent of the girls were white, 62 percent were single and 21 percent married (legally or consensually), and

relatively few had any serious physical handicap. Fifty percent had been previously committed to a venereal disease hospital, 9 percent as many as 4 times. In the families of 66 percent, serious social problems existed such as alcoholism, desertion, dependency, promiscuity and crime. Sixteen percent of the group had had no education, 36 percent had not gone beyond the third grade, 3 percent had gone beyond the eighth grade. Fifty-one percent had had previous vocational training, such as sewing and domestic service. For women outside of prostitution the earnings for 29 percent of the group were under \$10 per week, and for 25 percent under \$5 per week; only 1 percent earned \$10 or more per week.

The age of first sex experience was 15 years in 24 percent (64 percent were 15 years old or younger); 36 (15 percent) were initiated into prostitution at the age of 17 years, and 52 (21 percent) at 20 years or older. Of the 244 women classified as prostitutes, 146 (58 percent) had been in prostitution for 1 year or less; 24 (11 percent) for 2 years; 18 (8 percent) for 3 years.

Thirty-six percent stated that they intended to continue in prostitution; only 1 percent of the 38 percent who stated that they intended to quit had plans for the future.

The conclusions based on these findings are that social rehabilitation prospects are good for about one-third to one-half of the 280 girls, if provided with facilities for training, guidance, social case work, and employment. In 39 percent rehabilitation prospects were considered good, in 3 percent excellent, and in 6 percent no rehabilitation was necessary. It is the opinion of those making the survey that a well planned vocational guidance and training program supplemented by social case work would be successful in the rehabilitation of a substantial proportion of the women now engaged in prostitution in Puerto Rico.



legislative measures against the spread of venereal diseases in Sweden. Rolf J. M. Hallgren. Pub. Health, London, 57: 96-99, June 1944.

A brief resumé is given of the control measures used since the eighteenth century against the spread of venereal diseases. The Venereal Diseases (Prevention) Act adopted in 1918 is still in force. Due to an increase in the incidence of these diseases during the past 2 years, the government is considering recommendations for tightening up the procedure for dealing with the medical as well as the social aspects of the venereal disease problem. An outline of the present law together with the proposed recommendations is given. Briefly, the proposed recommendations include (1) the increase in the number of clinics with larger staffs; (2) social workers at the clinics in the large cities to investigate sources of infection; (3) increased use of the powers conferred on authorities by the Venereal Diseases Act to enforce isolation in hospital of recalcitrant persons; (4) establishment of free prophylactic treatment centers for men; (5) use of prophylaxis; (6) a widespread educational campaign by means of radio, newspapers, lectures and motion pictures; (7) compulsory instruction in sex physiology and ethics in the schools; (8) cooperation between the medical and social authorities.

A tabulation of the reported cases of venereal disease in Sweden from 1918 to 1943 shows that in 1918 a total of 4,256 cases of acquired syphilis was reported with a gradual decrease to 273 cases in 1941 and an increase to 936 in 1943. There were 16,626 cases of gonorrhea reported in 1918 which decreased to 10,006 in 1940, and then increased to 19,841 in

1943. There were 3,163 cases of chancroid reported in 1918 and 28 in 1941. In 1942 there were 35 cases; no figure is given for 1943. The four largest cities in Sweden are primarily responsible for the increase in gonorrhea in the past 2 years, with Stockholm having 35.4 percent of the total 10,006 cases in 1940.

**Syphilis in industry.** Rhode Island M. J., Providence, 27: 289, 292, June 1944.

This article stresses the important role of the routine serologic test in preemployment examinations in industry.

In the Collyer Insulated Wire Works of Pawtucket, routine serologic tests have been a part of the preemployment examinations since October 1942. Out of 1,175 persons examined, only 35 (0.033 percent) were found to be positive. These cases were all noninfectious and employable. They were referred to the family physician and followed up at quarterly or 6-month intervals.

**A health study of South African Bantu school-children.** Sidney L. Kark and H. le Riche. South African M. J., Cape Town, 18: 100-103, Mar. 25, 1944.

During 1938-1939 a health study was carried out among school children in the Transvaal, Orange Free State, Natal and Cape Province sections of South Africa. Approximately 7,000 children were given a physical examination, and laboratory tests were made on a random sample of children in each area. The Wassermann reaction was determined by the South African Institute for Medical Research. The results showed no difference in incidence between the total urban and rural groups examined, which were 23.60 percent and 23.28 percent positive, respectively.

**New Cases of Syphilis and Gonorrhea in States, Territories, Possessions and Panama Canal Zone**  
**Health officers' monthly statement: Report for July 1944 and 1943**

Area	Cases of syphilis and gonorrhea reported for July											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital			
	1944	1943	1944	1943	1944	1943	1944	1943	1944	1943	1944	1943
United States†	129,252	141,914	15,945	16,698	18,101	111,508	111,852	118,188	11,014	11,245	123,872	124,872
Alabama-----	1,158	1,658	171	229	233	346	204	416	16	43	496	616
Arizona-----	197	371	68	74	69	106	48	147	11	17	99	21
Arkansas-----	642	853	95	107	217	284	271	296	27	26	270	41
California-----	2,542	2,852	469	405	586	629	1,373	1,628	77	94	3,355	2,111
Colorado-----	197	458	66	114	57	136	66	192	8	16	229	211
Connecticut-----	215	278	20	29	112	96	45	102	5	6	91	111
Delaware-----	80	94	20	9	27	17	24	7	4	1	29	41
Dist. Columbia-----	107	730	11	114	25	194	55	389	5	10	67	341
Florida-----	1,215	2,330	205	260	383	697	505	954	24	38	1,177	1,431
Georgia-----	847	1,827	263	318	370	790	182	669	32	50	331	961
Idaho-----	78	52	19	45	15	3	43	3	1	0	66	21
Illinois-----	1,874	2,547	279	310	431	613	1,094	1,562	70	62	1,834	2,131
Indiana-----	461	724	88	100	79	43	140	290	22	16	270	291
Iowa-----	128	228	31	52	35	58	55	101	2	8	213	141
Kansas-----	252	170	47	33	57	23	133	107	15	7	182	101
Kentucky-----	416	872	103	78	104	162	167	344	28	37	357	311
Louisiana-----	1,015	1,749	242	301	316	540	243	563	43	53	1,223	1,061
Maine-----	73	72	14	16	10	11	30	31	11	6	199	91
Maryland-----	699	1,298	128	133	192	168	151	220	22	12	469	731
Massachusetts-----	303	363	72	88	(§)	(§)	211	259	20	16	356	381
Michigan-----	1,386	1,646	178	215	439	452	518	769	43	46	893	931
Minnesota-----	187	236	38	27	16	31	117	160	9	14	200	191
Mississippi-----	1,806	2,451	584	773	522	773	589	807	111	98	2,699	2,561
Missouri-----	813	632	196	109	212	165	363	298	23	30	614	401
Montana-----	27	33	6	4	1	5	9	19	1	0	26	31
Nebraska-----	110	85	9	16	29	54	64	10	5	4	92	101
Nevada-----	58	37	19	0	0	9	19	25	3	3	44	31
New Hampshire-----	30	15	2	3	1	10	23	2	2	0	14	31
New Jersey-----	675	824	120	113	179	237	351	438	19	36	520	381
New Mexico-----	128	174	35	28	25	46	53	88	15	12	136	101
New York-----	2,262	3,444	415	475	457	628	1,318	2,212	53	90	1,167	1,701
North Carolina-----	723	1,167	298	234	265	475	144	438	16	20	979	911
North Dakota-----	24	19	2	4	1	5	11	7	2	1	34	31
Ohio-----	1,425	1,894	297	253	380	514	690	1,045	58	82	796	391
Oklahoma-----	628	735	123	101	166	191	203	280	19	32	646	411
Oregon-----	186	173	54	43	25	11	102	118	5	1	240	201
Pennsylvania-----	1,031	1,264	167	155	310	510	359	496	28	52	0	91
Rhode Island-----	63	93	19	6	1	13	33	62	4	4	142	51
South Carolina-----	754	1,567	183	286	256	713	261	494	19	43	485	681
South Dakota-----	39	54	4	12	23	4	9	22	3	6	44	21
Tennessee-----	1,456	1,780	186	283	565	680	639	742	55	52	1,060	1,331
Texas-----	1,422	2,237	236	258	469	522	492	791	51	56	841	731
Utah-----	68	80	18	15	3	8	47	56	0	1	58	61
Vermont-----	15	15	2	3	5	5	7	6	1	1	37	31
Virginia-----	857	1,255	233	393	353	472	246	331	16	36	376	1,061
Washington-----	(*)	421	(*)	67	(*)	113	(*)	177	(*)	8	(*)	71
West Virginia-----	356	308	67	47	31	51	22	65	3	5	331	191
Wisconsin-----	62	92	25	14	0	0	35	77	2	1	78	111
Wyoming-----	162	78	18	13	49	8	88	50	5	1	7	111
<i>Territories, Possessions, and Panama C. Z.</i>												
Alaska-----	13	9	0	4	4	0	1	1	1	1	73	51
Canal Zone-----	67	(*)	7	(*)	13	(*)	41	(*)	2	(*)	53	(*)
Hawaii-----	82	85	26	15	18	9	33	53	2	7	126	111
Puerto Rico-----	945	766	158	143	308	131	280	245	188	86	567	201
Virgin Islands-----	16	25	1	5	7	16	2	2	1	1	7	31
Actual total† of U.S., Territories and Pan. Canal Zone-----	30,375	43,220	6,137	6,933	8,451	11,777	12,209	18,666	1,208	1,348	24,698	26,071

\*Data not available.

\*\*Includes "not stated."

†Based on States reporting in each year.

‡Includes all reported cases.

§Based on 47 States and D.C.



# New Cases of Syphilis and Gonorrhea in Cities of 200,000 Population and Over

Health officers' monthly statement: Reported for July 1944 and 1943

City	Cases of syphilis and gonorrhea reported for July											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and latent		Congenital		1944	1943
	1944	1943	1944	1943	1944	1943	1944	1943	1944	1943		
Total †	110,603	114,307	2,065	1,767	2,476	3,544	4,785	6,722	252	299	7,337	7,165
Albany.....	82	89	17	6	11	31	45	50	9	2	67	54
Albany.....	155	276	34	70	54	94	63	111	4	1	261	93
Atlanta.....	415	996	109	93	99	96	134	164	4	8	210	251
Baltimore.....	316	502	33	33	88	130	73	118	5	14	51	99
Birmingham.....	112	144	23	36	80	0	0	75	6	4	130	118
Boston.....												
Buffalo.....	128	149	14	13	15	35	95	98	4	3	72	43
Chicago.....	1,252	1,304	203	210	308	351	700	706	41	37	1,150	1,234
Cincinnati.....	169	199	27	30	(§)	(§)	142	169	0	0	56	51
Cleveland.....	288	300	70	43	97	107	113	140	8	10	142	93
Columbus.....	90	115	24	20	20	29	43	61	3	5	30	32
Dallas.....	186	250	44	61	57	45	85	143	0	1	71	89
Dayton.....	94	119	10	18	26	32	51	66	7	3	62	21
Denver.....	104	215	24	48	38	60	30	96	3	5	96	136
Detroit.....	941	1,108	159	124	343	322	422	638	17	24	530	569
Honolulu.....	21	53	7	11	3	8	10	29	1	5	65	118
Houston.....	126	174	29	32	50	66	44	68	3	8	178	183
Indianapolis.....	142	199	29	53	16	1	37	29	1	2	39	9
Jersey City.....	39	60	2	9	12	15	20	43	5	3	5	1
Kansas City.....	121	131	26	18	26	16	62	91	3	6	76	74
Los Angeles.....	852	988	362	0	0	362	469	606	21	20	426	362
Louisville.....	78	398	24	25	14	48	35	120	4	0	86	88
Memphis.....	538	697	42	79	245	329	239	283	12	6	401	504
Milwaukee.....	32	40	10	4	0	0	21	35	1	1	78	49
Minneapolis.....	59	68	21	15	11	15	27	37	0	0	84	79
Newark.....	146	180	34	27	44	49	67	99	1	5	114	72
New Orleans.....	290	336	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	383	87
New York.....	1,632	2,316	354	357	396	516	826	1,356	40	63	1,167	1,197
Oakland.....	121	167	14	12	28	44	74	107	5	4	133	127
Oklahoma Cy.....	162	148	50	22	44	43	43	73	3	5	0	81
Omaha.....	51	38	2	2	14	33	33	1	2	2	31	40
Philadelphia.....	389	321	46	36	39	183	134	1	3	8	29	18
Pittsburgh.....	(*)	792	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)
Portland.....	67	88	25	19	12	5	29	64	1	0	111	90
Providence.....	28	38	4	2	1	2	19	31	0	1	5	14
Rochester.....	14	18	3	2	1	0	10	15	0	1	33	5
St. Louis.....	556	436	115	64	159	158	267	201	15	13	332	165
St. Paul.....	22	25	7	7	4	9	7	6	2	2	8	41
San Antonio.....	115	147	17	13	22	41	73	92	3	1	80	118
San Diego.....	154	124	15	10	45	25	79	82	9	7	114	65
San Francisco.....	239	297	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	186	165
Seattle.....	79	116	16	11	18	25	40	72	0	1	124	147
Syracuse.....	33	83	3	1	1	3	29	76	0	3	34	23
Toledo.....	57	125	6	17	10	22	40	81	1	5	20	7
Wash'n, D. C.....	107	730	11	114	25	194	55	389	5	10	67	353
Actual total†	10,603	15,099	2,065	1,767	2,476	3,544	4,785	6,722	252	299	7,337	7,165

\*No data available.

\*\*Includes "not stated."

†Based on cities reporting in both fiscal periods.

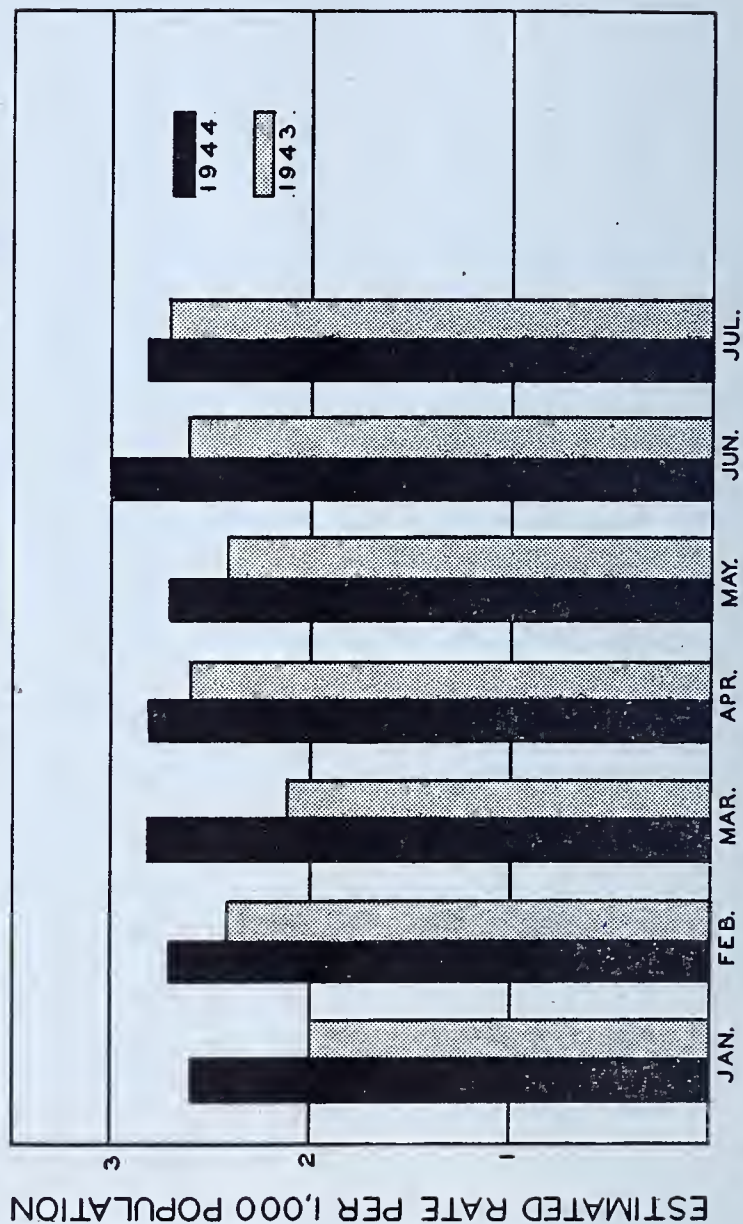
‡Includes all reported cases.

§Included in late and late latent.

¹Based on 43 cities.

²Based on 41 cities.

ANNUAL GONORRHEA CASE RATES  
IN CITIES OF 200,000 POPULATION AND OVER  
BASED ON PROVISIONAL MONTHLY DATA, 1944 AND 1943





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FEDERAL SECURITY AGENCY  
UNITED STATES PUBLIC HEALTH SERVICE

THOMAS PARRAN, *Surgeon General*

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# Cardiolipin Antigens in the Kolmer Complement Fixation Test for Syphilis

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United States Public Health Service

The report of the isolation and purification of cardiolipin (1) described this substance as a "new phospholipid from beef heart powder" which yielded "fatty acids and a phosphorylated polysaccharide." This substance was further identified as being "essential for the reactivity of beef heart antigens in the serologic tests for syphilis." A previous report of the serologic activity of cardiolipin antigens (2) indicated that cardiolipin, lecithin and cholesterol were not of themselves antigenic but that when these components were assembled in certain definite proportions antigenic activity equal to that of a previously accepted standard antigen was obtained. It was also stated that lecithin purified from petroleum ether (3) when obtained from either beef heart or eggs gave identical results.

The problem of producing antigens of constant reactivity from successive lots of beef heart powder by other published methods (4,5) has been fraught with many difficulties. Even under carefully controlled conditions of extraction and handling it was not always possible to obtain satisfactory antigens by these methods. As the efficiency of a complement fixation test for syphilis is to a great extent dependent on the antigen employed, the use of chemically identifiable substances such as cardiolipin and lecithin, which could be readily reproduced, might contribute much toward the stabilization of this phase of the serodiagnosis of syphilis. For this reason an investigation of the antigenicity, anticomplementary activity, keeping qualities and other properties of cardiolipin antigens in the Kolmer complement fixation test for syphilis was conducted.

The Kolmer complement fixation technic was used in this study because it was the complement fixation testing method most generally used by the United States Public Health Service laboratories and other laboratories serviced by the Staten Island laboratory at this time.

## REAGENTS AND METHODS

Cardiolipin and lecithin were prepared from beef heart in accordance with the methods described by Pangborn (1). Cholesterol obtained from Pfanstiehl marked "ash free (pptd. from alcohol)" was used in all cardiolipin antigens. Saline solutions contained 8.5 gm. C.P. sodium chloride and 0.1 gm. C.P. magnesium sulfate in 1,000 ml. distilled water. All other reagents employed and temperatures and time intervals adhered to were those listed under the Kolmer complement fixation tests for syphilis in Supplement No. 11 to Venereal Disease Information, June 1940, unless otherwise stated.

## ANTIGENIC ACTIVITY OF CARDIOLIPIN, LECITHIN AND CHOLESTEROL MIXTURES

Solutions of cardiolipin, lecithin and cholesterol, in absolute alcohol, were mixed in the proportions listed in table 1 and then stored in the dark in screw-top bottles at room temperature. Each of these solutions will be referred to by the antigen number recorded in this table. The control antigen used was a Kolmer antigen that had been in use at this laboratory and which was considered to be of standard reactivity. All antigens were tested in doubling dilutions from 1-75 to 1-2400. Every antigen dilution was individually prepared by slowly dropping antigen into saline solution.

From the Venereal Disease Research Laboratory, U. S. Marine Hospital, Staten Island, N. Y.

Table 1.—Composition of cardiolipin antigens

Antigen No.	Cardiolipin Percent	Lecithin Percent	Cholesterol Percent
21	0.03	0.05	0.3
22	0.03	0.05	0.6
23	0.03	0.05	0.9
24	0.03	0.5	0.3
25	0.03	0.5	0.6
26	0.03	0.5	0.9
27	0.03	5.0	0.3
28	0.03	0.05	0
29	0.03	0.5	0
30	0.03	5.0	0
31	0.03	0	0.3
32	0.03	0	0.6
33	0.03	0	0.9
34	0.06	0.05	0.3
35	0.15	0.05	0.3
36	0.3	0.05	0.3
37	0.06	0	0.3
38	0.15	0	0.6
39	0.3	0	0.6
40	0.3	0.05	0.6
41	0.06	0.05	0.6
42	0.06	0.05	0.9
43	0.3	0	0

To determine the capacity of each antigen to fix complement in the presence of constant amounts of positive serum of decreasing potencies, doubling dilutions of positive serum in negative serum were prepared for these tests. The reagent content of the particular positive serum used for this study allowed serum mixtures containing 1 part of positive with 4 parts of negative to 1 part of positive with 79 parts of negative serum to be used. After adequate dispersion, each of these serum mixtures was inactivated and tested in 0.2 ml. amounts. Anticomplementary controls for each dilution of every antigen and for all serum mixtures as well as the usual hemolytic system controls were included. Complement diluted 1-43 and hemolysin in 1-4000 dilution were employed throughout. The results are presented in table 2.

These results indicate that the greatest quantities of complement were fixed, in the tubes containing the lesser amounts of positive serum, by antigens 21, 22, 23, 34, 41 and 42. The factor common to each of these antigens was the quantity (0.05 percent) of lecithin contained. All of the antigens tested, which contained a greater proportion of this component, yielded a lesser maximum fixation of complement.

Antigens 21, 22 and 23 gave approximately equal degrees of complement fixation, at equivalent dilutions, although the

cholesterol content of these antigens was 0.3, 0.6 and 0.9 percent, respectively. This seems to indicate that the complement binding properties of these antigens, in the presence of positive serum, is not noticeably enhanced by increases of cholesterol content beyond 0.3 percent. The anticomplementary activity of these antigens, as portrayed by the antigen control titrations, was minimal and the anticomplementary properties of the other antigens did not follow the increases of cholesterol content. This suggests that the total anticomplementary properties of some antigens is not a function of the cholesterol per-

The effects of various cardiolipin proportions can be visualized from the results obtained with antigens 21, 34, 35 and 36, containing 0.03, 0.06, 0.15 and 0.3 percent cardiolipin, respectively, with constant amounts of lecithin and cholesterol. The two antigens containing the lesser amounts of cardiolipin, 21 and 34, appeared to have similar antigenic activity, but antigens 35 and 36, containing the larger amounts of cardiolipin, fixed less complement in the presence of positive serum and were demonstrably anticomplementary. Antigens 35 and 42, containing 0.06 percent cardiolipin with lecithin and 0.6 and 0.9 percent cholesterol, respectively, yielded slightly greater fixation of complement than any of the other antigens tested and showed minimal anticomplementary properties.

These results indicate that antigens of various reactivities can be prepared from cardiolipin, lecithin and cholesterol by altering the proportion of each of the constituents. Antigens having acceptable sensitivity will be found in the group containing 0.03 to 0.06 percent cardiolipin, 0.05 to 0.6 percent cholesterol and approximately 0.05 percent lecithin. This does rule out the probability that satisfactory antigens can be composed of greater concentrations of each of these components as long as the proportional relationship of each reagent to the other is retained. Movements in this direction are restricted by the concentrations of the parent solutions of cardiolipin, lecithin and cholesterol from which these antigens are assembled and by the solubilities of the 3 ingredients.



TABLE 2.—*Fixation of complement by various dilutions of antigen in the presence of constant amounts of serum of decreasing potency*

Parts Serum Neg.	75	150	300	600	1200	2400	75	150	300	600	1200	2400
None*	—	—	—	—	—	—	—	—	—	—	—	—
+	—	—	—	—	—	—	—	—	—	—	—	—
79	—	—	—	—	—	—	—	—	—	—	—	—
39	—	—	—	—	—	—	—	—	—	—	—	—
19	—	—	—	—	—	—	—	—	—	—	—	—
9	—	—	—	—	—	—	—	—	—	—	—	—
4	—	—	—	—	—	—	—	—	—	—	—	—
Antigen 21	—	—	—	—	—	—	—	—	—	—	—	—
Antigen 22	—	—	—	—	—	—	—	—	—	—	—	—
Antigen 23	—	—	—	—	—	—	—	—	—	—	—	—
Antigen 24	—	—	—	—	—	—	—	—	—	—	—	—
Antigen 25	—	—	—	—	—	—	—	—	—	—	—	—
Antigen 26	—	—	—	—	—	—	—	—	—	—	—	—
Antigen 27	—	—	—	—	—	—	—	—	—	—	—	—
Antigen 28	—	—	—	—	—	—	—	—	—	—	—	—
Antigen 29	—	—	—	—	—	—	—	—	—	—	—	—
Antigen 30	—	—	—	—	—	—	—	—	—	—	—	—
Antigen 31	—	—	—	—	—	—	—	—	—	—	—	—
Antigen 32	—	—	—	—	—	—	—	—	—	—	—	—
Antigen 33	—	—	—	—	—	—	—	—	—	—	—	—
Antigen 34	—	—	—	—	—	—	—	—	—	—	—	—
Antigen 35	—	—	—	—	—	—	—	—	—	—	—	—
Antigen 36	—	—	—	—	—	—	—	—	—	—	—	—
Antigen 37	—	—	—	—	—	—	—	—	—	—	—	—
Antigen 38	—	—	—	—	—	—	—	—	—	—	—	—
Antigen 39	—	—	—	—	—	—	—	—	—	—	—	—
Antigen 40	—	—	—	—	—	—	—	—	—	—	—	—
Antigen 41	—	—	—	—	—	—	—	—	—	—	—	—
Antigen 42	—	—	—	—	—	—	—	—	—	—	—	—
Antigen 43	—	—	—	—	—	—	—	—	—	—	—	—
Kolmer (V. D. Lab.) antigen	—	—	—	—	—	—	—	—	—	—	—	—

\*These tubes contained only antigen, complement and saline and served as anticomplementary antigen controls.

4, 3, 2, 1, and ± indicate the degree of inhibition of hemolysis as included in the Kolmer test outline.

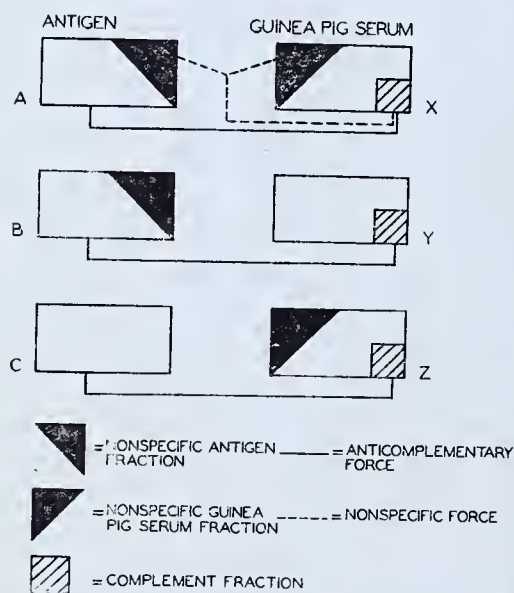
— indicates complete hemolysis.

All tests were placed at 6° C. for 16 hours and were read after a secondary incubation of 1 hour at 37° C.

# ANTICOMPLEMENTARY AND NONSPECIFIC PROPERTIES OF CARDIOLIPIN ANTIGENS

For the purposes of this investigation the anticomplementary and nonspecific behavior of antigens in the Kolmer test is divided into three phases. These divisions include the anticomplementary activity at 37° C. and at 6° C. and the nonspecific destruction of complement at 6° C.

Determination of the anticomplementary capacity of a lipoidal serologic antigen at refrigerator temperature is complicated by the fact that complement from some guinea-pig serums may be partially or wholly fixed at this temperature in the presence of antigen (6). Thus an antigen may exhibit the ability to deviate complement nonspecifically from one guinea-pig serum yet fail to do so from another. This capacity is dependent on the antigen-guinea-pig-serum combination employed (7) and appears to follow the behavior pattern of an antigen-antibody complex. An illustration of this relationship is contained in a graph.



This hypothecation visualizes the non-specific deviation of the complement fraction of a guinea-pig serum by the complex formed of the nonspecific fractions of the antigen-serum combination as being a force independent of the direct anticomple-

mentary action of an antigen. The term "nonspecific" has been applied to this reaction because it occurs to a greater degree at low temperatures than at 37° C. since it is zonal in nature, being evidenced in dilution ranges far removed from the anticomplementary titer, and in order to differentiate this phenomenon from the direct anticomplementary action of antigen alone.

Of the antigen-complement combination presented in the graph antigen A plus guinea-pig serum X could be expected to show the greatest complement destruction when tested at refrigerator temperature. In this combination the complement destroyed would be an indication of the combined effects of the nonspecific fraction of the antigen, and the direct anticomplementary action of the antigen, and would therefore be more pronounced than would be expected if this same antigen were tested with guinea-pig serum Y. This latter instance would more truly exhibit the anticomplementary action of antigen. However, if antigens A and B were tested with guinea-pig serum Y these antigens might give identical reactions and the ability of antigen A to nonspecifically deviate complement would not be observed because the necessary nonspecific serum fraction would be missing from these combinations.

For these reasons, two types of complement serum were obtained for the testing of the cardiolipin antigens. One of the serums, which will be referred to as complement 1, was a pooled serum from guinea pigs whose individual serums were found to allow the deviation of their complement nonspecifically when tested with an antigen having this capacity. The other complement serum, designated as complement 2, was a pooled serum from 8 guinea pigs having no detectable nonspecific properties.

Although the antigen control tube readings in table 2 give some indication of the relative anticomplementary capacity of each of the antigens tested, the excess complement contained in these tests obscured the destruction of small amounts of this reagent. In order to survey more critically the anticomplementary powers



These antigens each antigen was tested in the presence of smaller amounts of guinea-pig serum. For this purpose only those antigens previously found to possess adequate complement fixing capacities in the presence of positive serum were tested.

This group was composed of antigens 21, 22, 23, 41, 42 and a Kolmer antigen which were tested in dilutions ranging from 1-10 and 1-2400 with complements 1 and 2. The results of these tests are presented in table 3.

TABLE 3.—*Titrations to determine anticomplementary and nonspecific properties of antigens in various dilution zones*

Complement 1, ml. of 1-30 dil.	Antigen dilutions, 1 part to—							Antigen dilutions, 1 part to—						
	10	25	75	150	300	600	1200	10	25	75	150	300	600	1200
Antigen 21														
0.8	±	—	—	—	—	—	—	1	—	—	—	—	—	—
0.6	2	—	—	—	—	—	—	4	—	2	—	—	—	—
0.4	4	—	—	—	—	—	—	4	—	—	—	—	—	—
Antigen 23														
0.8	3	—	—	—	—	—	—	2	—	—	—	—	—	—
0.6	4	—	—	—	—	—	—	3	1	—	—	—	—	—
0.4	4	±	—	—	—	—	—	4	3	—	—	—	—	—
Antigen 42														
0.8	4	1	—	—	—	—	—	4	—	—	—	2	—	1
0.6	4	2	—	—	—	—	—	4	2	—	—	—	3	2
0.4	4	4	±	—	—	—	—	4	4	—	—	—	3	3
Kolmer antigen*														
Antigen 22														
0.8	±	—	—	—	—	—	—	1	—	—	—	—	—	—
0.6	2	—	—	—	—	—	—	4	—	—	—	—	—	—
0.4	4	—	—	—	—	—	—	4	—	—	—	—	—	—
Antigen 41														
0.8	3	—	—	—	—	—	—	2	—	—	—	—	—	—
0.6	4	—	—	—	—	—	—	4	±	—	—	—	—	—
0.4	4	±	—	—	—	—	—	4	3	—	—	—	—	—
Antigen 42														
0.8	4	1	—	—	—	—	—	4	—	—	—	—	—	—
0.6	4	2	—	—	—	—	—	4	1	—	—	—	—	—
0.4	4	4	±	—	—	—	—	4	2	—	—	—	—	—
Kolmer antigen*														
Complement 2 ml. of 1-30 dil.														
Antigen 21														
0.8	±	—	—	—	—	—	—	1	—	—	—	—	—	—
0.6	2	—	—	—	—	—	—	4	—	—	—	—	—	—
0.4	4	—	—	—	—	—	—	4	—	—	—	—	—	—
Antigen 23														
0.8	3	—	—	—	—	—	—	2	—	—	—	—	—	—
0.6	4	—	—	—	—	—	—	4	±	—	—	—	—	—
0.4	4	±	—	—	—	—	—	4	3	—	—	—	—	—
Antigen 42														
0.8	4	1	—	—	—	—	—	4	—	—	—	—	—	—
0.6	4	2	—	—	—	—	—	4	1	—	—	—	—	—
0.4	4	4	±	—	—	—	—	4	2	—	—	—	—	—
Kolmer antigen*														

\*This antigen gave negative reactions in all 3 tubes in 1-2400 and 1-4800 antigen dilutions, with complements 1 and 2.

The anticomplementary effects of antigens 21, 22 and 23 were evidenced only in the lower antigen dilutions (1-10) with both complements, while the anticomplementary actions of antigens 41 and 42 were discernible in the next higher dilutions tested. Approximately the same degree of anticomplementary reactivity was obtained with the Kolmer antigen in the lower antigen dilutions, but this antigen also exhibited a zone of complement deviation in the higher antigen dilutions with complement 1, thereby establishing its nonspecific capacity. As not any of the cardiolipin antigens tested gave zonal complement destruction in the higher antigen dilutions under the conditions of this test with either complement serum, it is evident that the tendencies of these antigens to react nonspecifically, if present at all, were below the level of detection by this procedure.

The slight increase of anticomplementary activity obtained with antigens 41 and 42 indicates that cardiolipin antigens similar to 21, 22 and 23 would be preferred on this basis.

If acceptable cardiolipin antigens are found to be relatively free of this nonspecific factor, the use of these antigens in the Kolmer complement fixation test would eliminate the need for pretesting of complement or the use of egg white solution. In order to further explore this possibility, serums from 167 guinea pigs were individually pretested, as previously reported (7), using antigens 21, 22, 23, 41, 42 and a Kolmer antigen. All of these serums yielded essentially negative results with the 5 cardiolipin antigens, and 137 negative reactions were obtained with the Kolmer antigen. The 30 serums which showed some degree of nonspecific complement

fixation in the presence of the Kolmer antigen gave negative pretest reactions with the cardiolipin antigens, so would have been considered satisfactory sources of complement for tests employing these latter antigens.

The ability of an antigen to destroy complement during a 1-hour primary incubation at 37° C. must also be considered as this is the condition under which the comple-

ment is titrated for the Kolmer complement fixation test for syphilis. To investigate this phase of antigen behavior complement titrations were performed according to the Kolmer technic on 8 individuals and 12 pooled lots of complement serum with the 5 cardiolipin antigens and a Kolmer antigen prepared in the laboratory. The results of one of these titrations, representative of the group, are given in table 4.

TABLE 4.—Kolmer complement titration

Antigen	Dilution	Tube readings						Complement titer
21	1-150	—	—	—	—	1	2	1-37
22	1-150	—	—	—	—	1	2	1-37
23	1-150	—	—	—	—	1	2	1-37
41	1-150	—	—	—	±	1	2	1-33
42	1-150	—	—	±	1	2	4	1-30
41	1-300	—	—	—	—	±	2	1-37
42	1-300	—	—	—	—	±	2	1-37
Kolmer (V. D. Lab.)	1-600	—	—	—	—	±	2	1-37

The test dose optimum for each antigen, as previously determined (table 2), was used for these tests. This choice allowed antigens 41 and 42 to be used in 1-300 dilution and antigens 21, 22 and 23 in 1-150 dilution. Antigens 41 and 42 at 1-150 dilution were also included to ascertain if the small difference in anticomplementary potentialities between these antigens and antigens 21, 22 and 23 at the same dilution would be evidenced in this titration. Identical complement titrations were obtained in each instance when antigens were

employed at their optimum titers so that on this basis alone each of the antigen tested would be equally acceptable.

SPECIFICITY AND SENSITIVITY OF CARDIOLIPIN ANTIGEN

The 370 blood specimens received at this laboratory during the 1944 National Serologic Evaluation Survey were tested by the Kolmer method employing cardiolipin antigen 21 and a Kolmer (V. D. Laboratory) antigen. In these tests, identical amounts of all reagents were used with

TABLE 5.—Results of Kolmer complement fixation tests performed at the Venereal Disease Research Laboratory, Staten Island, N. Y., on specimens received in the 1944 National Serologic Evaluation Survey

Syphilitic group								
Antigen	Serums tested	Negative		Doubtful		Positive		Sensitivity
		Number	Percent	Number	Percent	Number	Percent	Percent
Kolmer 21	216	31	14.4	9	4.2	176	81.5	83.6
	211	30	14.2	11	5.2	170	80.6	83.2
Nonsyphilitic group								
Antigen	Serums tested	Negative		Doubtful		Positive		Specificity
		Number	Percent	Number	Percent	Number	Percent	Percent
Kolmer 21	159	0	0	1	0.6	158	99.4	99.7
	159	0	0	0	0	159	100.0	100.0



ch antigen and the tests employing both antigens were performed simultaneously. Antigen 21 was used for these comparative testings because preliminary tests had indicated that its level of reactivity would approximate that of the Kolmer antigen in use at this laboratory.

The figures in table 5 show that the results obtained with these 2 antigens on this group of specimens were similar. On identical serums in the syphilitic group of specimens, 15 slightly weaker and 13 slightly stronger reactions were obtained with the cardiolipin antigen 21. The only discrepancy in the nonsyphilitic group occurred with 1 specimen which gave a doubtful reaction with the Kolmer antigen and was negative with antigen 21. This cardiolipin antigen had been in storage at room temperature for 1 year prior to its use in this survey.

#### STABILITY OF CARDIOLIPIN ANTIGENS

The tests listed in table 2 were again performed on all antigens listed in table 1 after these antigens had been stored in the dark at room temperature for 1 year. These comparative results were so similar to the original findings listed that their presentation is omitted. On this basis it is considered that not any detectable deterioration of these antigens had occurred during the storage period. The behavior of antigen 21 in the National Serologic Evaluation Survey lends additional evidence in support of this assumption.

These antigens were stored in bottles with screw tops (plastic) containing tin oil liners and had been opened three times during the storage period. Opportunity for evaporation and exposure to light was minimized during this test period by replacing the top as soon as antigen had been removed, being certain that the top was screwed on tightly and by replacing the bottle into a dark container.

Concentrations that might occur if bottles of these antigens were left open for longer periods of time at more frequent intervals would undoubtedly change the reactivity level of the antigen and possibly cause precipitates to form when maximum

solubilities were exceeded. Such changes have not been observed in this laboratory with other cardiolipin antigens which have been opened as many as 30 times during a 1-year period.

#### DISCUSSION

Each of the components of cardiolipin antigens appears to have certain definable influences on antigen behavior. The cardiolipin fraction in addition to supplying the determining factor of specific fixation also contributes much toward the anticomplementary capacity of an antigen when present in certain concentrations. In this connection, it was noted that when the cardiolipin portions of antigens were increased sufficiently, anticomplementary properties were more evident and the maximal specific fixabilities of these antigens were diminished. However, the optimal concentration of each of the cardiolipin antigen components may be varied somewhat since their effects are interdependent.

The higher percentages of cholesterol employed did not appear to contribute much more to antigen activity than did the lesser amounts used. These findings are not in agreement with observations of the effects of increased cholesterolization on Kolmer antigen reactivity. As cholesterol may be serving only as an activator either by chemical union or in the formation of particles, its effect on cardiolipin antigens may be limited by the fact that a definite amount of only one reactive substance is present. In antigens containing two or more antigenic components, or a larger proportion of a single component, the amount of cholesterol needed for maximal activation might be in excess of 0.3 percent.

The effects of cardiolipin and cholesterol are restricted by the action of the lecithin present in cardiolipin antigens. Although a certain proportion of this substance is needed to complete the cardiolipin antigens, an excess is definitely deleterious to antigenic activity. This may be one reason why certain Kolmer antigens are found to be deficient in specific fixability. However, the complement fixation patterns presented by the antigens tested indicate that a sero-

logic antigen of predictable behavior can be assembled from the three cardioli-  
pin components.

The ability of cardioli-  
pin antigens to deviate complement nonspecifically is minimal. Kolmer antigens have been found to possess varying capacities in this direction. Such antigens received from other laboratories for standardization have, when tested with individual guinea-pig serum, shown nonspecific fixation of complement with as many as 95 to as few as 5 from each 100 serums tested. It had been previously noted that antigens prepared from some lots of commercial beef heart powder contained more of this undesirable characteristic than did Kolmer antigens prepared from other lots of powder. It was also found that repeated extraction of the beef heart powder with acetone prior to the alcoholic extraction tended to diminish the nonspecific potency of the antigen. Beef heart from which cardioli-  
pin and lecithin are procured is first liberally extracted with acetone so this may be one point at which much of this nonspecific antigen component is eliminated.

Serologic reactions also commonly referred to as being nonspecific are ones wherein a positive test is obtained on a specimen from a presumably nonsyphilitic donor. It is not expected that this type of reaction can be entirely eliminated by the use of cardioli-  
pin antigens since cardioli-  
pin is probably one of the principal antigenic lipoids of beef heart and may, therefore, be responsible for some such reactions by any antigen prepared from this source. Cruder antigens may, however, yield a greater number of such false positive reactions if they contain other substances which are of themselves antigenic. Other factors which will influence the number of false positive reactions obtained are the test sensitivity threshold, which in complement fixation tests is mainly determined by the amount of complement employed and the quantity of antigen used. Adjustments of this nature may alter test specificity in a quantitative rather than a qualitative manner by increasing or decreasing the number of positive reactions obtained in both the syphilitic and nonsyphilitic donor groups.

The standardization of antigens used in complement fixation tests for syphilis would materially assist in establishing test reproducibility between laboratories. Kolmer antigens prepared from different lots of beef heart powder may have such dissimilar reactivities that identical potencies cannot be obtained even though these antigens be employed at different dilutions. This may in part, be due to the dissimilar proportions of lecithin, cardioli-  
pin and other antigenic components present in the alcoholic extracts from which these antigens are prepared. Difficulties of this nature are not encountered in the assembly of cardioli-  
pin antigens since this involves only the mixing of cardioli-  
pin and lecithin solutions in predetermined proportions and the addition of cholesterol. However, the purification of cardioli-  
pin and lecithin are involved procedures that can best be accomplished under the supervision of a chemist.

Findings that recommend cardioli-  
pin antigen for use in the Kolmer complement fixation test for syphilis, are reproducibility, adequate sensitivity without excessive anticomplementary activity, and the minimal degree of nonspecific complement deviation.

#### SUMMARY AND CONCLUSIONS

1. Tests were made to determine the specific fixability of cardioli-  
pin antigens of varied composition.
2. A titration method to differentiate the anticomplementary and nonspecific properties of antigens is described.
3. Specificity and sensitivity ratings of the Kolmer test employing a cardioli-  
pin antigen in the 1944 National Serology Evaluation Survey are presented.
4. Storage for 1 year at room temperature had no detectable effect on the serologic efficiency of the cardioli-  
pin antigen tested.

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## Trend in Age of Acquiring Venereal Disease in New York City 1940-1943

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It frequently has been stated that since the entrance of the United States into the war the age of acquiring venereal disease has been lowered. This paper presents corroborative data for the years 1940 through 1943, showing the age distribution of reported cases of primary or secondary syphilis and gonorrhea in New York City. Since primary or secondary syphilis and gonorrhea are newly acquired infections, they may be used as an index of the trend in incidence of these diseases.

Observations in clinics and in hospitals treating early syphilis and gonorrhea would indicate that there has been a rise in new infections, rather than more complete reporting. Examination of table 1 indicates that although reported cases of primary and secondary syphilis have increased, reported cases of syphilis in later stages have shown no changes comparable to those which have occurred in new infections. The increase in early latent cases in 1941 over 1940 does not entirely represent a greater rate of infection, but is the result of Selective Service examinations which were begun in November 1940 and which sought to light many latent and unsuspected infections. The number of cases of early latent syphilis reported in the male decreased from 1,554 in 1940 to 2,218 in 1941, while the number in the female in-

creased only from 2,244 to 2,502. Cases of late or late latent syphilis decreased in 1941 compared with 1940, the decrease in cases in the female being greater than in the male, but in 1942 reported cases in the male increased from 10,844 to 12,108, while the number of cases in the female decreased. In 1942 the extension of Selective Service examinations to include older men, because the United States had entered into the war, resulted in an increase in the discovery of cases of late latent syphilis. In 1943, both sexes decreased in approximately the same proportion. Reported cases of congenital syphilis have steadily declined as the result of the intensive efforts made in past years to treat pregnant women. Cases reported without a definite diagnosis decreased in 1941 because of greater efforts on the part of the Health Department to have all reporting agencies give a complete diagnosis. These efforts could not be continued in 1942 because of increased work brought on by the war, and, therefore, the number of cases reported without a definite stage increased. In 1943 efforts were resumed to obtain a complete diagnosis, resulting in a decrease in cases incompletely reported.

In tables 2 and 3 is shown the actual number of cases of primary or secondary syphilis and gonorrhea reported in each age group by sex, and the percentage distribution for the years 1940 through 1943. Primary or secondary syphilis cases show numerical increases in almost every age group. However, disregarding the actual

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TABLE 1.—*Reported cases of venereal disease by sex in New York City, 1940-1943*

	1940	1941	1942	1943
Total syphilis.....	30,718	27,194	30,036	25,878
Primary or secondary.....				
Male.....	2,066	2,040	2,338	2,757
Female.....	1,041	917	1,076	1,495
Early latent.....				
Male.....	1,554	2,218	2,459	2,726
Female.....	2,244	2,502	2,815	2,825
Late or late latent.....				
Male.....	11,380	10,844	12,108	9,526
Female.....	8,470	6,961	6,836	5,480
Congenital.....				
Male.....	456	382	387	279
Female.....	683	584	557	372
Stage not given.....				
Male.....	1,482	452	934	299
Female.....	1,342	294	526	119
Gonorrhea.....				
Male.....	10,751	9,196	9,336	9,619
Female.....	3,888	3,101	2,686	3,338
Chancroid.....				
Male.....	280	412	500	371
Female.....	8	18	30	39
Granuloma inguinale.....				
Male.....	41	88	84	80
Female.....	14	10	12	17
Lymphogranuloma venereum.....				
Male.....	183	214	184	145
Female.....	75	78	57	42

TABLE 2.—*Age distribution of reported cases of primary or secondary syphilis in New York City, 1940-1943*

Age	MALE				FEMALE			
	1940	1941	1942	1943	1940	1941	1942	1943
Total.....	2,066	2,040	2,338	2,757	1,041	917	1,076	1,495
Under 15 years.....	3	5	4	4	11	11	11	14
15-19.....	120	132	177	306	141	123	154	305
20-24.....	483	448	596	795	348	301	364	543
25-29.....	426	449	461	511	220	212	222	288
30-34.....	326	354	364	365	111	101	129	152
35-39.....	255	241	277	253	83	62	65	76
40-44.....	176	151	174	195	54	54	43	37
45-49.....	113	111	106	129	22	19	26	21
50-54.....	59	58	68	71	11	8	15	15
55 years and over.....	52	49	51	59	5	6	6	6
Age unknown.....	53	42	60	69	35	20	41	38
Percentage distribution*..	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Under 15 years.....	0.1	0.3	0.2	0.1	1.1	1.2	1.1	1.0
15-19.....	6.0	6.6	7.8	11.4	14.0	13.7	14.9	20.9
20-24.....	24.0	22.4	26.2	29.6	34.6	33.6	35.2	37.3
25-29.....	21.2	22.5	20.2	19.0	21.9	23.6	21.4	19.8
30-34.....	16.2	17.7	16.0	13.6	11.0	11.3	12.5	10.4
35-39.....	12.7	12.1	12.2	9.4	8.2	6.9	6.3	5.2
40-44.....	8.7	7.5	7.6	7.3	5.4	6.0	4.1	2.5
45-49.....	5.6	5.6	4.6	4.8	2.2	2.1	2.5	1.4
50-54.....	2.9	2.9	3.0	2.6	1.1	0.9	1.4	1.0
55 years and over.....	2.6	2.4	2.2	2.2	0.5	0.7	0.6	0.4
Median age (in years)....	29.7	29.6	28.9	27.3	25.1	25.3	24.8	23.8

\* Does not include age unknown.



TABLE 3.—*Age distribution of reported cases of gonorrhea in New York City, 1940-1943*

Age	MALE				FEMALE			
	1940	1941	1942	1943	1940	1941	1942	1943
Total.....	10,751	9,196	9,336	9,619	3,888	3,101	2,686	3,338
Under 15 years.....	84	72	72	59	355	323	249	171
15-19.....	983	901	1,218	1,743	337	287	380	581
20-24.....	3,210	2,930	3,134	3,490	1,288	1,067	956	1,219
25-29.....	2,528	2,079	1,992	1,801	872	593	537	602
30-34.....	1,541	1,339	1,135	1,062	451	394	271	346
35-39.....	972	765	741	612	269	187	139	206
40-44.....	578	463	404	307	129	108	53	102
45-49.....	335	236	203	144	83	60	32	44
50-54.....	164	119	127	67	29	32	19	25
55 years and over....	138	119	87	67	29	19	7	18
Age unknown.....	218	173	223	267	46	31	43	24
Percentage distribution*..	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Under 15 years.....	0.8	0.8	0.8	0.6	9.2	10.5	9.4	5.2
15-19.....	9.3	10.0	13.4	18.6	8.8	9.3	14.4	17.5
20-24.....	30.5	32.5	34.4	37.3	33.5	34.8	36.2	36.8
25-29.....	24.0	23.0	21.9	19.3	22.7	19.3	20.3	18.2
30-34.....	14.6	14.8	12.5	11.4	11.7	12.8	10.3	10.4
35-39.....	9.2	8.5	8.1	6.5	7.0	6.1	5.3	6.2
40-44.....	5.5	5.1	4.4	3.3	3.4	3.5	2.0	3.1
45-49.....	3.2	2.6	2.2	1.5	2.2	2.0	1.2	1.3
50-54.....	1.6	1.3	1.4	0.7	0.8	1.0	0.7	0.8
55 years and over....	1.3	1.3	1.0	0.7	0.8	0.6	0.3	0.5
Median age (in years)....	27.0	26.5	25.3	24.1	24.8	24.3	23.6	24.5

\* Does not include age unknown.

numbers and considering only the percentage distribution, there is a distinct lowering of the age when syphilis or gonorrhea is acquired. In primary or secondary syphilis the median age for the male is about the same in 1940 and 1941 but shows a decrease of 2.3 years from 1941 to 1943. The median ages for the female are also approximately equal in 1940 and 1941, but show a decrease of 1.5 years from 1941 to 1943. In gonorrhea in the male there is a steady decline in median age, the difference from 1941 to 1943 being 2.4 years. However, in the female there is a downward trend from 1940 to 1942 and then an increase in 1943, with 1943 being 0.2 years greater than 1941.

During the 4 years for both sexes in primary or secondary syphilis and in gonorrhea, the proportion of cases in the two age groups, 15-19 and 20-24 years, has increased. The largest increase has been in the 15-19-year-age group. The proportion of cases in this group for the male with primary or secondary syphilis

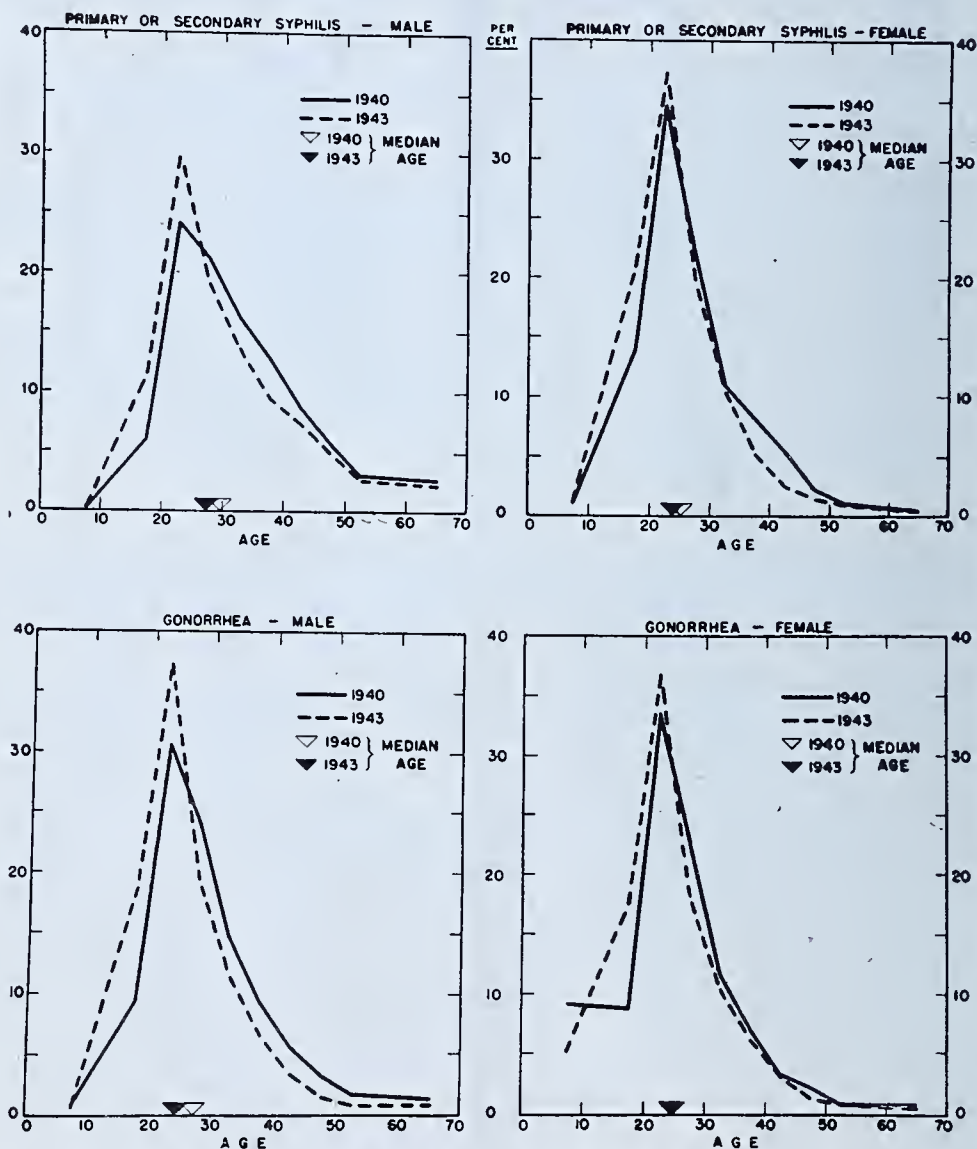
has increased 90 percent from 1940 to 1943, for the female 49 percent; for the male with gonorrhea 100 percent and for the female 99 percent. The proportion of cases in the age group 20-24 years with primary or secondary syphilis has increased 23 percent for the male and 8 percent for the female; in gonorrhea 22 percent for the male and 10 percent for the female. The percentage of cases in the other age groups, with a few minor exceptions in those having few cases, has decreased.

In each sex and disease the largest number of cases is found in the age group 20-24 years. Except for cases of primary or secondary syphilis in the female in 1943, the next largest number is in the age group 25-29 years. In 1940 and 1941 the third largest group in either sex for gonorrhea is in the 30-34-year-age group. In 1942 and 1943 this latter group is relegated to fourth position, with the 15-19-year-age group going into third place. In primary or secondary syphilis in the male, the 30-34-year-age group is the third largest,

# PERCENTAGE DISTRIBUTION OF REPORTED CASES OF PRIMARY OR SECONDARY SYPHILIS AND GONORRHEA

BY AGE AND SEX

1940 AND 1943





with the 15-19-year-age group in sixth position in 1940 through 1942, but taking fourth place in 1943. The 15-19-year-age group is the third largest for primary or secondary syphilis in the female, except, as mentioned above, in 1943, when it was second.

Some of the cases reported without a definite stage of syphilis may have been in the primary or secondary stage, but they have not been included in this study. If all these cases were included as primary

or secondary syphilis, the median ages shown in table 2 would become:

	1940	1941	1942	1943
Male .....	33.4	31.3	30.9	28.0
Female .....	28.0	26.4	26.1	23.9

The relative decline in median ages would then be even greater than in table 2. Moreover, the increase in the percentage of cases falling in the 15-19- and 20-24-year-age groups would be more pronounced, as shown in the following table:

	Primary or secondary syphilis only			Primary or secondary syphilis and unknown stage combined		
	1940	1943	Difference	1940	1943	Difference
Male—15-19 years.....	6.0	11.4	5.4	4.3	10.8	6.5
20-24 years.....	24.0	29.6	5.6	17.9	27.8	9.9
Female—15-19 years.....	14.0	20.9	6.9	9.1	20.3	11.2
20-24 years.....	34.6	37.3	2.7	26.3	36.3	10.0

The accompanying chart illustrates graphically the changes between 1940 and 1943. For each disease and sex there is an increase in the proportion of cases in the younger ages with a resulting relative decrease in those in the older ages. The largest number of cases is always in the 20-24-year-age group. This group and the 15-19-year-age group have increased from 1940 through 1943. The median age in each group is lower in 1943 than in 1940, with the difference more marked in the male than in the female.

*Summary.*—Study and analysis of cases of new venereal disease infections reported

to the New York City Health Department for the years 1940 through 1943 show a lowering of the median age for primary or secondary syphilis from 29.7 to 27.3 years for the male and from 25.1 to 23.8 years for the female, and for gonorrhea in the male from 27.0 to 24.1 years. Gonorrhea in the female declined from 24.8 years in 1940 to 23.6 years in 1942, but increased to 24.5 years in 1943.

The percent of cases in the age groups 15-19 and 20-24 years has increased, with the greatest increase in the former group. However, the largest number of cases still occurs in the 20-24-year-age group.

## The Effect of Penicillin on the Development of the Primary Lesion of Syphilis: Case Report

Earl C. Van Horn, Major, and Theodore R. Dakin, Captain, Medical Corps,  
U. S. Army

A 28-year-old soldier appeared in the Outpatient Venereal Disease Clinic, Camp Atterbury, on June 13, 1944, with acute gonorrhea. The blood Kahn reaction was negative at that time. He was treated with sulfathiazole for 5 days on duty status. On June 19, the soldier still had a discharge and was admitted to Wakeman General Hospital, where the blood Kahn reaction was reported negative on June 21. On June 22, he received 100,000 units of penicillin

which was given intramuscularly (20,000 units every 3 hours) with no reaction. The patient's response to this medication was good and he was discharged to duty on June 27, after 3 negative spreads and 1 negative culture for gonorrhea had been obtained.

Investigation of the source of the patient's infection revealed that he had contacted the same woman on several occasions, the last being June 3, without using

prophylaxis. On July 7, a report was received from the Isolation Hospital, Indianapolis, Ind., stating that the woman from whom the soldier had contracted gonorrhea also had early infectious syphilis. The soldier was placed under observation. On July 25, a small penile ulcer, 0.5 x 1 cm. in diameter, was noted at the base of the frenulum. Darkfield examination of material from this ulcer was positive for *Treponema pallidum* on July 27; the Kahn reaction was negative on July 26. Diagnosis of "new" syphilis, primary, positive darkfield and negative Kahn reaction, was made on July 27 and treatment started. He gave no history of previous syphilitic infection or treatment.

The incubation period in this case was 52 days or longer. It is apparent from the case reported that treatment with 100,000 units of penicillin during the incubation period did not prevent the development of the primary lesion of syphilis. It is entirely possible that further observations on the administration of penicillin during the incubation period will show that its administration during that period results in the same confusion in regard to therapy as was experienced when prophylactic arsenical injections were in use.

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## DIAGNOSIS

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**Syphilis among soldiers.** (Erfahrungen über Syphilis an einem grösseren Soldatenkrankengut.) Arnold Spinner. Med. Klin., Berlin, 40: 288-290, 1944.

Among a total of 363 cases of syphilis found among soldiers, 213 (58.7 percent) were primary syphilis, 73 (20.1 percent) were secondary syphilis, and 77 (21.2 percent) were latent syphilis. The number of cases of congenital syphilis, tertiary syphilis, and metasymphilis was comparatively small and is not included in this study.

The sources of infection were wife 3.4 percent; fiancée or steady girl friend 0.9 percent; pick-up 68.4 percent; prostitute 27.3 percent. The soldiers were unable to give the name of the pick-up in 66.2 per-

cent of cases; for that reason these contacts could not be traced. Of the infections 67 percent occurred among the common soldiers, 24.5 percent among noncommissioned officers, and 8.5 percent among sergeant-majors.

In spite of the propaganda for it, prophylaxis still is not popular among the soldiers, with the exception of condoms which are widely used. It has been observed that so-called "condom chancres," located at the base of the penis in an area where there is no condom protection, occur quite frequently.

Alcohol played an important role in contraction of syphilis in that it removed inhibitions and made contact easier.

Infections were reported as soon as they were discovered by 75 (36.5 percent) men with primary and 49 (72.3 percent) men with secondary syphilis; within 1 week by 92 (45.5 percent) men with primary and 18 (24.7 percent) men with secondary syphilis; within 2 weeks by 34 (14.8 percent) men with primary and 3 (1.5 percent) with secondary syphilis; within 3 weeks or slightly later by 12 (3.2 percent) men with primary and 3 (1.5 percent) with secondary syphilis, and reported after a still longer interval by 138 (63.5 percent) men with primary and 24 (27.7 percent) men with secondary syphilis.

In 85 percent of cases the primary lesion was located on the prepuce; only 1 extragenital lesion was found which occurred on the lower lip; multiple chancres were found in 44 percent of cases. The dark-field examination was positive in all but 3 cases on first examination.

In 22 cases, gonorrhea was also present; in 6 of these the primary lesion of syphilis appeared after treatment for gonorrhea had been completed. Chancroid was found in 4 cases. It is advised that blood serologic reactions be carried out more frequently to detect cases of latent syphilis. In this series of latent syphilis 61 (79.2 percent) cases were found on admission to the hospital, 13 (16.9 percent) on premarital examination, 2 (2.6 percent) on blood donor examination, and 1 (1.3 percent) on examination of kitchen personnel.



he influence of fever reactions on the *Spirochaeta pallida* and on the manifestations produced by the Unna-Ducrey Streptobacilli, as well as their role in the diagnosis of mixed chancre. (Der Einfluss von Fieberreaktionen auf die *Spirochaeta pallida* und auf die durch Unna-Ducreysche Streptobazillen hervorgerufenen Erkrankungen sowie ihre Rolle in der Diagnostik des gemischten Schankers.) S. Bugarski. Dermat. Wchnschr., Leipzig, 116: 158-161, 1943. Abs. Zentralbl. f. Bakt., Jena, 144: 266, 1944.

The author points out the following facts which are of value in the diagnosis of mixed chancre: The febrile reactions produced by means of drugs have a considerable influence on the disappearance of *Spirochaeta pallida* from the lesions, whereas the febrile reactions produced by non-specific vaccines do not have this effect and have only an insignificant influence on the disappearance of the symptoms of chancroid. However, the febrile reactions produced by the intravenous administration of Unna-Ducrey Streptobacillus vaccine have a considerable effect on chancroid and its complications as well as on the chancroid component of the mixed chancre without affecting the spirochete content of the mixed chancre. The intravenous injection of this Streptobacillus vaccine is therefore of great value in the diagnosis of mixed chancre.

**False positive serologic reactions for syphilis. Report of 100 cases following routine immunizations and upper respiratory infections.** A. B. Loveman. Bull. U. S. Army M. Dept., Carlisle Barracks, No. 80: 95-106, Sept. 1944.

The author reports the results of a study of 100 patients with positive serologic reactions for syphilis seen during an epidemic of upper respiratory infections (nasopharyngitis) among troops at Fort Jackson, S. C., who had recently received routine Army immunizations.

The plan of study included a complete history and a thorough physical examination. If a false positive serologic reaction was suspected, quantitative Kahn and Wassermann tests were performed weekly

for at least a month, when another physical examination was made. If the serologic test remained positive, the patient was followed (some as long as 6 months) until a diagnosis could be made as to the presence or absence of syphilis. The average time from the first immunization to the first positive serologic reaction was 32 days (longest 120 and shortest 5 days). In over 90 percent of the cases there was no evidence of syphilis.

Ninety-seven percent of the patients denied a history of penile lesions, 93 percent stated that serologic tests in the past had been negative, and 85 percent that their tests were negative when inducted. A history of upper respiratory infection and recent immunization was given in 86 percent of the cases.

The Kahn test remained positive for a longer period than the Wassermann test. The Kahn quantitative titer was of definite value in differentiating true from false positive types of reactions.

In these cases, clinical evidence based on an accurate history and physical examination was more dependable than the initial serologic test. The author is of the opinion that if the evidence points against a diagnosis of syphilis when a serologic test for syphilis is repeatedly positive, the patient should be carefully investigated and the serologic data appraised for as long as 6 months, if necessary, before instituting treatment for syphilis.

**False positive serology in infectious hepatitis.** News and comment. Bull. U. S. Army M. Dept., Carlisle Barracks, No. 80: 4, Sept. 1944.

Of 63 patients with infectious hepatitis among allied military personnel in Sicily, 15 showed false positive or doubtful positive serologic reactions after the clinical appearance of jaundice (serologic studies were not made prior to the onset of jaundice). In 8 or 9 cases, when both the Kahn and Wassermann tests were performed, the Kahn test was more strongly positive and remained so for a longer time.

In a study of 20 cases showing false positive reactions, there was a pronounced

trend toward negativity in the third week after icterus appeared; only 7 remained positive after the third week; 1 case was faintly positive in the seventh week.

#### **Granuloma venereum: A cause of death.**

**Report of six fatal cases.** Edgar R. Pund and George F. McInnes. *Clinics, Philadelphia*, 3: 221-234, June 1944.

It is agreed that granuloma inguinale is a venereal disease which is transmitted by direct contact. The external genitals and the inguinal region are the most common sites of inoculation; the cervix, uterus, and tubes may become involved by extension of the lesion. Autoinoculation may explain secondary lesions in other portions of the body. Donovan bodies have been demonstrated in the regional lymph nodes.

The authors review 6 cases which definitely indicate that granuloma inguinale may sometimes prove fatal. This is especially true in women during childbearing age when cervical lesions may extend to the uterus, tubes, and ovaries. Four of the 6 deaths reported occurred in women between the ages of 21 and 28, and in 3 of these the internal genitals were involved and in all the symptoms dated from abortions or deliveries. When complicated with granuloma inguinale of the cervix pregnancy is especially hazardous. When the 24 cases of granuloma inguinale of the cervix which are in the authors' files are considered, the 3 deaths with extension to the internal genitals represent a mortality rate of 14.3 percent.

Two of the deaths occurred in male Negroes. When 1 of these patients was first seen he gave a history of inguinal ulceration for 8 months. He was admitted to the hospital in a state of extreme emaciation and polyavitaminosis and died 14 days later. Necropsy showed extensive ulceration involving both inguinal regions and the medial side of both thighs. Numerous Donovan bodies, both intracellular and free, were observed and there was a superimposed fusospirochetosis. The other male patient was observed at irregular periods for 7 years. At first the entire penis was involved; after 5 years there was dirty ulceration of both lips which extended over

the buccal mucosa, gums, palate, and into the pharynx. Biopsy revealed granuloma inguinale and Donovan bodies. He had been given antisyphilitic therapy because of a positive Kahn reaction. He died from cardiac failure with contributing inanition resulting from his inability to take food because of the oral and esophageal lesions.

Secondary infections, especially spirochetosis, possibly were contributing factors in 4 of these cases; positive Wassermann reactions were obtained in 2 cases.

Careful search was made for Donovan bodies. In no instance was there evidence of hematogenic spread. In 1 case the encysted Donovan bodies were observed, for the first time, in giant cells of the foreign body type and it may, therefore, be assumed that the pathognomonic cell is a histiocyte.

#### **Polyarticular arthritis and osteomyelitis due to granuloma inguinale.** John Lyford, III, Roger B. Scott and Robert W. Johnson. *Am. J. Syph., Gonorr. & Ven. Dis., St. Louis*, 28: 588-610, Sept. 1944.

Three cases of polyarticular arthritis and osteomyelitis caused by granuloma inguinale have been described. In 1 instance, there was a systemic dissemination of the disease with a massive polyarticular arthritis and, ultimately, ulceration of many of the joints, and a widespread destruction of the bones. (This case was reported by the authors in *Bull. Johns Hopkins Hosp.*, 74:213-217, 1944.) In the second case, there was involvement of 2 vertebrae and a hip joint communicating with sinus tracts presenting in the inguinal regions. The third patient had lesions in the bones of a hand and forearm, but no joint involvement.

The fact that no member of any of these patients' families developed granuloma inguinale would suggest that infection involves more than mere contact with material from an active lesion.

These cases add further proof that granuloma inguinale can be a systemic as well as a local disease. In the cases in which blood chemical studies were made there was a reversal of the albumin/glo-



bulin ratio with an increase in the blood serum globulin. All patients showed a persistent anemia, and the courses in all were marked by a gradual loss in weight. All the patients had irregular spiking temperatures over a long period of time. The activity of the lesions and the systemic manifestations were marked by recurring episodes of spontaneous remissions and exacerbations.

The arthritis presented a picture of an insidious onset with migratory pains in several joints, then swelling of several joints with pain locally but little free fluid. With rest of the affected joints, there was a slow subsidence into a typical "rheumatoid arthritis," followed by a recurrence of the acute swelling and pain of multiple joints, and ending after many months in ulceration from within outward of many of the joints. Exploration of an elbow joint during the period of quiescence showed the synovia to be thickened and friable, but the articular cartilages were clean and smooth. The operative incision into the infected tissue of the joint healed per primam and remained healed.

Radiographic examination of the bone lesions revealed little or no sequestrum or involucrum formation, and a lytic type of reaction. At operation and in prepared specimens, the lesions contained no "pus" and consisted of friable granulation tissue.

Microscopic examination disclosed Donovan bodies in material from the bone and joint lesions in 2 cases, and in material from the sinus tracts communicating with the involved bones in the third case. The organisms could be seen readily in specimens prepared by the routine method for microscopic study, and stained with hematoxylin and eosin by the usual technic.

No satisfactory explanation for the mode of spread of the Donovan bodies within the host could be given in these cases, but the massive involvement of the bones and joints in 1 case suggests that the spread could be hematogenous.

In 1 of the 2 instances in which continuous tissue cultures of material from the lesions were attempted, typical Donovan bodies grew for several weeks in the cultures of material from both the bone

and joint. The potentialities of the method of continuous tissue cultures as an approach to the study of other types of arthritis should be considered.

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## TREATMENT

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### Intensive chemotherapy of early syphilis.

Arthur W. Neilson, Loren F. Blaney, Leroy J. Stephens and Richard W. Maxwell. *Am. J. Syph., Gonorr. & Ven. Dis., St. Louis, 28: 553-570, Sept. 1944.*

From October 1940 to March 1943 intensive mapharsen therapy for early syphilis was completed 502 times on 487 patients at the St. Louis Isolation Hospital. The treatment routine used closely followed that originally outlined by Chargin, each patient receiving from 900 to 1,200 mg. in an average of 5 days. In over one-half of the cases insoluble bismuth was added in an attempt to create a chemotherapeutic regimen of maximum effectiveness.

The majority of all reactions to treatment were immediate and were due to mapharsen, except for local reaction at the site of bismuth injections. Four (0.76 percent) case fatalities resulted, which are discussed in detail with a report of autopsy findings. The most common reaction to intravenous mapharsen was pain in the arm at the point of injection, and next in frequency nausea and vomiting in 54 percent.

Of the first 414 patients treated, 159 (37.4 percent) failed to report once to the follow-up clinic, and many others made only one or more visits.

The time interval between treatment and the achievement of a negative Kahn reaction averaged 4.3 months in the group receiving mapharsen alone, and 2.8 months in the group that received bismuth in addition to mapharsen.

Of 155 patients, treated with mapharsen or mapharsen combined with bismuth, 23 (15 percent) developed serologic or mucocutaneous relapse, many of whom were given a second course of intensive treatment.

Twenty pregnant women were given

therapy, and 17 were followed until delivery had occurred. Only 2 infants had definite congenital syphilis, and 2 babies had positive Kahn reactions (under 3 months of age).

Although the follow-up of these cases receiving intensive chemotherapy for early syphilis has not yet been long enough for a proper evaluation of the results, the authors believe that the rate of complete cure will be at least 70 percent.

**Review of 2,144 courses of rapid treatment for early syphilis.** Evan W. Thomas and Gertrude Wexler. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, 28: 529-552, Sept. 1944.

From December 1939 to March 1944, a total of 2,023 patients at Bellevue Hospital were given 2,144 treatment courses, using the authors' method of rapid therapy for early syphilis. Of the total number of treatment courses, 321 consisted of mapharsen only, 1,634 of mapharsen and typhoid vaccine, 120 of mapharsen and fever induced by electropyraxia, and 69 of the Eagle plan of treatment. The maximum single dose per day was fixed at about 1 mg. mapharsen per kilogram of body weight given over a period of at least 10 days and combined with 4 fevers induced by typhoid vaccine. Later 4 injections of 0.1 gm. bismuth salicylate in oil were added during the 10-day period.

Before this present schedule of treatment went into effect, of 909 treatment courses during which 2 injections of mapharsen had been given on at least 1 day of the treatment course, the incidence of encephalopathy was over 1 percent and 3 of the patients died. The present schedule was adopted in July 1942 and by Mar. 1, 1944, a total of 1,046 treatment courses had been given without a single fatality and with only mild toxic reactions, with the exception of 1 case of agranulocytosis in which recovery took place.

In a total of 2,144 rapid treatment courses, the incidence of encephalopathy was higher among men than among women. The authors found no relationship between menstruation and arsenical encephalopathy.

The authors' findings indicate that the

general pattern of quantitative serologic tests for syphilis during and following rapid treatment suggests that a reagin may be produced for varying lengths of time after the spirochete has been killed, that is, the longer a patient has had syphilis the longer it takes for the serologic tests for syphilis to become negative.

Of the patients followed for 6 to 29 months after treatment, about 80 percent gave satisfactory results. If retreatments are included, satisfactory results were seen in 85.6 percent.

The most encouraging feature of the rapid treatment of early syphilis was the low incidence of positive spinal fluid findings in patients who have been followed from 6 months to 4 years after treatment.

Neurorecurrences following rapid treatment were fewer than with routine treatment.

**Penicillin.** 1. Prolonged action in beeswax-peanut oil mixture. 2. Single injection treatment of gonorrhea. Monroe J. Romansky and George R. Rittman. *Bull. U. S. Army M. Dept.*, Carlisle Barracks, No. 81: 43-49, Oct. 1944.

Twelve patients with gonococcic urethritis, 3 without previous treatment and 9 who were sulfonamide resistant, were treated with single injections of penicillin beeswax-peanut oil mixture. The doses varied between 51,250 and 100,000 Oxford units contained in 2 to 3 cc. of the beeswax-peanut oil mixture. The injections of this mixture produced and maintained levels of penicillin in the blood for from 7 to 10 hours. Potency was maintained at room, incubator, and refrigerator temperatures for from 30 to 62 days, and there was no sign of deterioration.

Of the 12 patients, 11 were cured as evidenced by freedom from clinical symptoms, and negative spreads and cultures at the end of 2, 5, and 7 days after treatment. Spreads and cultures taken hourly indicated that the group became negative at the fifth and seventh hour after the single injection of penicillin beeswax-peanut oil mixture. The 1 failure received the smallest dose of penicillin (51,250 O. u.)



but this does not explain the failure since the levels obtained in the blood compare favorably with the levels of patients who were cured and received larger doses. It is likely that the gonococcus was more resistant to the action of penicillin. There were no abnormal reactions.

#### **Penicillin for the treatment of chemo-resistant gonorrhea in the female.**

Robert B. Greenblatt and Anita R. Street. J. A. M. A., Chicago, 126: 161-163, Sept. 16, 1944.

A total of 109 women (84 white and 25 Negro) with gonorrhea was treated with penicillin. Of these, 93 percent had had one or more courses of sulfonamides. Several of the women received penicillin before having received a full course of sulfonamide therapy because of their sensitivity to sulfonamide drugs; some received no preliminary sulfonamide therapy. Penicillin was administered intramuscularly in aqueous or saline solution in doses of 10,000 to 20,000 Oxford units at 3-hour intervals to a total dosage of from 60,000 to 150,000 O. u. One patient with concomitant granuloma inguinale received 1,000,000 O. u. No untoward reactions resulting from penicillin therapy were observed. Following penicillin therapy, 4 or more cultures were taken in 85 percent of the cases. Cultures were taken daily for the first few days and then at intervals of 1, 2, or more days. In 3 patients no follow-up cultures were obtained. Five patients received a second course of penicillin because positive cultures were obtained after a period of 5 or more days following the administration of the first course. The total dosage given in the second course was from 120,000 to 300,000 O. u. In these 5 patients, 6 to 12 negative cultures were obtained after the second course.

A total of 551 women (46 percent white and 54 percent Negro) was studied for venereal diseases and in 61 percent laboratory evidence to support the diagnosis of gonorrhea was obtained. Proportionately, 1½ times as many white women received penicillin for chemoresistant gonorrhea, giving the impression that Negro women are more responsive to sulfonamides than

white women. The author suggests that a total dose of not less than 150,000 O. u. be given in the treatment of gonorrhea in order to prevent the development of penicillin-resistant strains of gonococci.

#### **The treatment of sulfonamide resistant gonorrhea with penicillin sodium.**

Thomas H. Sternberg and Thomas B. Turner. J. A. M. A., Chicago, 126: 157-161, Sept. 16, 1944.

Studies were carried out in 15 selected Army hospitals with a view toward determining as rapidly as possible time-dosage factors in the treatment of sulfonamide resistant gonorrhea with penicillin. A total of 1,686 patients refractory to at least 2 courses of a sulfonamide, and, in some cases, to artificially induced fever was treated with total dosages varying from 40,000 to 160,000 Oxford units per case, the individual dose being 10,000 or 20,000 units intramuscularly every 3 hours.

These studies showed penicillin to be a remarkably effective drug in the treatment of gonorrhea, usually causing disappearance of symptoms and reversal of bacteriologic findings within 48 hours. One course of treatment with a dosage of 160,000 units per case effected cures in 98 percent, 80,000 to 120,000 units in 96 percent, and 50,000 units in 86 percent. No significant differences in the final results were noted when a given total dose was administered in individual injections of either 10,000 or 20,000 units. Furthermore, little advantage was gained by prolonging the time of treatment schedules beyond 12 hours.

Factors such as duration of infection, previous fever therapy, and race appeared to have no effect on the results of therapy.

Of the total of 126 failures to 1 course of penicillin, 85 were retreated, using a 100,000 unit dosage. Of these, 78 (91.8 percent) were cured. Thus, by retreatment of failures with a second course, 99 percent cures were obtained. No case in the entire series proved to be penicillin resistant.

Complications of gonorrhea responded well to penicillin, although the more serious forms required prolonged treatment with higher dosage.

Reactions to penicillin were inconsequential, and in no instance was it necessary to discontinue treatment for this reason.

Because of the known effects of penicillin on *Treponema pallidum*, the possibility of masking or delaying the development of early syphilis must be considered.

In the discussion, Mahoney pointed out that the use of penicillin in the treatment of gonorrhea may have the effect of masking or greatly altering the symptoms of the invasion of a concomitantly acquired syphilis. He advises repeated serologic tests for syphilis for at least 2 months following treatment. The questions of total dosage, the duration of treatment, the interval between injections, and the number of injections cannot be considered as established at present, even in the light of the favorable results which have been reported.

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## LABORATORY RESEARCH

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**The susceptibility of sulfonamide-resistant gonococci to penicillin.** Arthur W. Frisch, Beatrice Behr, Robert B. Edwards and Marvin W. Edwards. *Am. J. Syph., Gonor. & Ven. Dis., St. Louis*, 28: 627-633, Sept. 1944.

The incorporation of penicillin directly into chocolate agar plates was employed to estimate the susceptibility of gonococci to this drug. A study of 181 sulfonamide susceptible or sulfonamide resistant patients revealed that all strains failed to grow on media containing 5 units per ml. of penicillin. In 66 similar cases, cultures were employed with media containing 1 unit of penicillin per ml. and in no instance was growth obtained on this concentration. From these data it is clear that most sulfonamide resistant gonococci are fully susceptible to penicillin. Pure culture studies showed that as little as 0.05 Oxford unit per ml. of media was sufficient to inhibit the growth of gonococci.

A total of 91 patients was followed at

intervals after treatment with penicillin. The gonococci disappeared from the urethra within 48 hours after treatment in 70 patients. Positive cultures were obtained 2 to 21 days after therapy in 19 patients who subsequently recovered. In 2 cases classed as therapeutic failures, cures were effected by elevation of the dosage.

The authors have been unsuccessful in the production of penicillin resistance by repeated transfer of cultures on gradually increasing concentrations of penicillin. Of 2 patients admitted to the hospital with a diagnosis of penicillin-fastness, one proved not to have gonorrhea, and cultures from the second were fully susceptible to the action of the drug.

**The enhancement of virulence of the gonococcus for the mouse.** C. Philip Miller and Edward Tamani. *Am. J. Syph., Gonor. & Ven. Dis., St. Louis*, 28: 620-626, Sept. 1944.

The virulence of a strain of gonococcus for white mice was enhanced by persistent animal passage until it reached a level which enabled inoculums of less than 10 gonococci to initiate lethal infections with regularity. One hundred and thirty animal passages during the course of 15 months were required to raise and stabilize its virulence at this level.

This strain surpassed all others in its response to mouse passage. Results with 10 others, out of a total of 70, were sufficiently successful to bring the minimum lethal doses within the range in which death could be the result only of a genuine infection rather than of the toxic action of the gonococci themselves.

The ability of the strain to retain virulence during subcultivation on artificial media increased gradually throughout the course of the series of animal passages. In the beginning each subculture resulted in appreciable loss of virulence, but toward the end of the series 4 subcultures could be interposed without loss of virulence. The experimental gonococcal infection produced by this strain proved highly satisfactory for testing in vivo such chemotherapeutic agents as the sulfonamides and penicillin.



Methods and media are described. Inoculations were made intraperitoneally with gonococci suspended in mucin. Death usually occurred between 18 and 36 hours. The pathologic changes were those of generalized sepsis.

**A carbohydrate-lipid fraction of gonococcus and meningococcus.** Alden K. Boor and C. Phillip Miller. *J. Infect. Dis.*, Chicago, **75**: 47-57, July-Aug. 1944.

Trichloroacetic acid was a very efficient agent in preparation of an opalescent, colloidal suspension of a carbohydrate-lipid complex, which the authors have designated "glucolipid," from certain gram-negative diplococci.

Among the genus *Neisseria* this extractable toxic, antigenic product varied in amount with species, strain, and physical and chemical pretreatment of cells. No difference was found in toxicity of like quantities of glucolipid from various strains of gonococci and meningococci, irrespective of bacterial virulence.

Serums from immunized rabbits exhibited excellent precipitating activity but mediocre agglutinating power against homologous strains. Mouse protection was sometimes good, but often not demonstrable.

Immunologically the glucolipid was not more than relatively specific among the gonococcus and meningococcus. The carbohydrate, separated from the lipid by acid hydrolysis, gave specific precipitin reaction with antiglucolipid and antibacterial serums.

**Statistical studies in female gonorrhea with an evaluation of yeast supplement in gonococcus isolation.** Philip Rosenblatt, Edda Meyer and Lillian Robbins. *Am. J. Syph., Gonorr. & Ven. Dis.*, St. Louis, **28**: 634-638, Sept. 1944.

The authors made a study to compare statistically proteose No. 3 hemoglobin agar (Bacto) with a similar medium fortified by the addition of Bacto-Supplement A (Difco). The latter material was used in a 1 percent concentration, and contained the yeast supplementary factors together

with crystal violet. The procedure followed in the preparation of the medium is described.

Tests were made on 141 female patients hospitalized for the treatment of gonorrhea, the diagnosis being made by spread or culture. All patients were treated with sulfonamides, and cultures and spreads were taken at 3-day intervals. In 776 cultures taken from the cervix uteri and urethra the fortified medium gave 3 times as many positive isolations as the chocolate agar, thus proving the former to be superior.

This study indicated that cultures from the cervix uteri were positive more often than cultures from the urethra. The correlation of spreads with positive cultures showed agreement in only 19 cases (13.6 percent).

This study shows that the chance of making a diagnosis of gonorrhea on a spread alone is somewhere in the ratio of 1 : 4. On the other hand, the specificity of cultures as against spreads is such as to discourage the use of spreads almost entirely in the diagnosis of gonorrhea in the female.

**The role of the liver and gallbladder in the excretion in the dog of some of the newer sulfonamides.** Harry Shay, S. A. Komarov, Herman Siplet and Samuel S. Fels. *Gastroenterology*, Baltimore, **2**: 432-435, June 1944.

Experimental studies were made by the authors to determine whether any of the known sulfonamides which produce low blood levels after clinical doses might not also be preferentially excreted by the liver, and so result in a concentration of the drug in hepatic and gallbladder bile as to make it suitable for the treatment of biliary tract disease. Experiments were made on dogs, using sulfaguanidine, sulfathiazole, sulfasuxidine and sulfathalidine.

From their experiments, the authors conclude that sulfathiazole is concentrated by the liver of a dog in a constant relationship to the blood level, the ratio being independent of the blood concentration. The introduction of the succinyl radical

into the sulfathiazole molecule at N<sup>4</sup> results in a considerable increase in the hepatic bile/blood concentration ratio, while the introduction of the phthalyl radical in the same position increases the ratio many times more so that the removal from the blood of the latter compound by the liver reaches a high degree of selectivity. Sulfaguanidine appears to be excreted by the liver at approximately the blood level. Sulfathalidine appears to be partially broken down in the dog's liver with the liberation of a free sulfonamide, presumably sulfathiazole.

The gallbladder of a normal dog concentrates sulfathiazole, sulfasuxidine, and sulfathalidine in proportion to water absorbed from the bile. It neither excretes nor absorbs any of these drugs, but is able to absorb sulfaguanidine.

This study is being extended to other sulfonamides.

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## PUBLIC HEALTH ADMINISTRATION

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**Annual report of the Surgeon General, U. S. Navy.** Statistics of diseases and injuries for the calendar year 1941. Washington, 1944.

*Venereal diseases (pp. 69-83).*—Venereal disease occupied second place among all causes of morbidity and contributed the fifth largest number of sick days of any group (except for 1930, it has been in second place since 1925). These diseases were the cause of 11.65 percent of all admissions and 6.38 percent of total sick days. The admission rate for 1941 was 51.05 per 1,000, 36.40 percent less than 1940. There were 2,390 new admissions for chancroidal infections, 12,687 for gonococcic infections, 2,298 for syphilis, 292 for lymphogranuloma venereum, 15 for verruca acuminata (venereal), and 131 for syphilis (seropositive only), making a total of 17,813 cases during the year. Adding 398 cases of venereal disease which were acquired prior to enlistment, the total venereal disease rate would be increased 1.14 per 1,000.

There were 192,868 sick days reported, and the daily average number of persons on the sick list was 1.51 per 1,000. This was 56.73 percent less than the median rate for the preceding 9 years (3.49). The noneffective ratio per 100,000 cases caused by chancroidal infections was 13.14; for gonococcic infections, 105.50; for syphilis, 24.71; for syphilis (seropositive only) 4.45. There were 16,738 sick days recorded for chancroidal infections, resulting in 6.2 sick days per case; 134,397 for gonococcic infections, or 8.61 per case; 31,474 for syphilis, or 11.5 per case; 5,668 for syphilis (seropositive only), or 17.07 per case; 350 for verruca acuminata (venereal), or 14.58 per case; 4,241 for lymphogranuloma venereum, or 13.0 days per case.

The rate for all venereal diseases per 1,000 admissions was 62.35 for the Navy and 48.69 for the Marine Corps. For the enlisted personnel the admission rate, as compared with the median rate of the preceding 9 years, showed for the Navy decreases of 28.45 for chancroidal infections, 31.49 for gonococcic infections, and 47.14 for syphilis; for the Marine Corps the corresponding decreases were 45.25, 35.18, and 43.90.

According to reports submitted on Dec. 31, 1941 by all ships and shore stations, there were 16,608 naval personnel with a history of syphilis. A total of 8,304 persons were treated with arsenical compounds during 1941. During the year, 22 reactions were reported following the use of arsenicals, with 1 death from cerebral hemorrhage following the administration of mapharsen.

**Annual report of the Surgeon General, U. S. Navy.** Statistics of diseases and injuries for the calendar year 1941. Washington, 1944.

*Comments of medical officers taken from annual sanitary reports (pp. 83-93).*—The greatest number of cases of gonorrhea on the U. S. S. Lexington occurred following exposures in the southern California area. Excellent results were obtained from the use of sulfathiazole. On the U. S. S. Nevada 90 percent of the infections occurred among men with more than 2 years'



service. In the Scouting Force, the admission rate for venereal diseases was phenomenally low in the Hawaiian area, very high in mainland ports, and still higher in Asiatic ports. More than one-third of the total admissions for the Force came from one cruiser as a result of a 2 weeks' visit to the mainland.

The medical officer for the Atlantic Fleet believes that the low rate for the Atlantic Coast is aided by (a) education of personnel and applications of preventive measures in ships, (b) civilian venereal disease control activities, and (c) the type of duty which curtailed liberty or shore leave. During 3 months in Iceland with liberty twice a week, there was 1 admission for venereal disease from local contacts reported by the U. S. S. Idaho. Among 88 liberty days in the Pearl Harbor-Honolulu area, there were 10 admissions for venereal disease, and among 77 liberty days in United States ports, 39 admissions.

Most of the shore stations have reported that the rate for venereal disease is very high. One station reported that 17 cases of syphilis in the Army and Navy had been traced to 1 woman, who was not a commercial prostitute. While several stations report that respiratory infections cause the greatest loss of time, gonorrhea was the largest single cause of illness and caused the greatest number of sick days at San Juan, P. R. Taxicabs cause much trouble at New River, N. C. Lectures are given and films shown, and prophylactic stations have been established.

**Venereal disease control.** Mississippi Doctor, Booneville, 22: 109-110, Sept. 1944.

During 1943 a little under 300 clinics were in operation in the State of Mississippi. Admissions were 23,019 patients with syphilis and 6,328 with gonorrhea. Of the 23,019 cases of syphilis, 2,075 were primary and secondary, 10,094 were early latent, 9,895 were late and late latent, and 955 were congenital. A high percentage of these cases were registrants, expectant

mothers, and contacts to military personnel; the cases of gonorrhea were mostly contacts to military personnel. In the clinics there were administered 643,498 doses of arsenicals, 680,249 doses of heavy metals, and 10,000 treatments (weekly) for gonorrhea. Physicians are requesting increasing quantities of therapeutic agents for syphilis.

The public health treatment centers admitted more than a thousand patients with syphilis and gonorrhea during the year. The majority of those admitted were infectious and sexually promiscuous.

There were 11,000 spinal punctures in 1943, compared with approximately 150 each year in the biennium 1939-41. This procedure is now a part of the management of clinic patients. In 1943, 1,400 patients were found to have positive spinal fluid reactions.

**Venereal disease quarantine upheld.** California's Health, Sacramento, 2: 26, Aug. 31, 1944.

The following opinion has been issued relative to the authority of health officers in California to quarantine individuals infected with a venereal disease in county or city jails:

"The legislature, recognizing the danger to the safety and welfare of the people in permitting persons afflicted or suspected of being afflicted with communicable diseases to run at large and expose the public to such communicable diseases, has by statute imposed upon each health officer of this State the mandatory duty of the quarantining of those persons afflicted or reasonably suspected of being afflicted with a communicable disease.

" \* \* \* city and county jails may be used for places of quarantine where no other public institutions are available for quarantine or where an emergency has arisen requiring the use of such jails or where the afflicted person is under confinement in the city or county jail and his quarantine in such city or county jail will not be detrimental to other prisoners."

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**New Cases of Syphilis and Gonorrhea in States, Territories and Possessions**  
Health Officers' monthly statement: Reported for the first two months of fiscal years  
1944-45 and 1943-44

Area	Cases of syphilis and gonorrhea reported for first 2 months of fiscal years below											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital			
	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44
Total U. S.†	60,107	84,981	12,588	13,427	16,595	23,127	24,480	36,804	12,197	12,500	52,552	50,933
Alabama.....	2,099	3,122	321	428	451	673	379	820	44	83	1,062	1,234
Arizona.....	411	590	126	130	124	159	116	232	43	20	209	323
Arkansas.....	1,333	1,581	249	220	440	577	522	540	52	48	684	819
California.....	5,645	5,699	1,059	799	1,252	1,318	3,064	3,260	178	198	7,932	4,515
Colorado.....	466	885	133	199	151	252	165	397	17	37	501	515
Connecticut.....	461	561	46	56	249	199	83	191	9	30	183	215
Delaware.....	134	217	34	19	46	45	42	25	4	4	55	55
Dist. Columbia...	176	1,485	19	199	44	368	88	842	7	24	171	515
Florida.....	2,739	5,655	455	538	904	1,733	1,118	2,645	53	106	2,783	2,915
Georgia.....	1,786	3,725	482	669	744	1,536	486	1,399	74	119	1,102	1,915
Idaho.....	183	87	48	56	43	12	87	16	4	0	116	116
Illinois.....	3,805	5,131	596	620	873	1,238	2,207	3,150	129	123	3,970	4,415
Indiana.....	983	1,337	209	177	122	105	340	526	43	43	608	515
Iowa.....	277	432	61	99	68	116	122	180	14	26	413	315
Kansas.....	474	415	107	70	96	74	249	255	22	16	453	315
Kentucky.....	935	1,488	215	174	222	315	374	605	54	63	838	615
Louisiana.....	2,188	3,175	488	545	693	919	512	1,065	84	92	2,840	2,015
Maine.....	180	165	39	41	22	18	61	81	15	14	366	215
Maryland.....	1,541	3,019	349	274	430	311	357	429	38	24	909	1,515
Massachusetts.....	696	781	168	169	(§)	(§)	481	580	47	32	782	715
Michigan.....	3,045	3,282	444	429	920	826	1,138	1,335	87	106	2,135	1,915
Minnesota.....	418	440	66	45	34	60	283	310	21	19	439	315
Mississippi.....	3,782	4,703	1,209	1,479	1,095	1,441	1,249	1,574	229	209	5,484	5,115
Missouri.....	1,682	1,437	406	251	442	384	713	650	50	54	1,335	815
Montana.....	67	75	20	24	5	6	19	37	2	2	61	61
Nebraska.....	207	183	27	33	54	106	116	31	7	7	357	215
Nevada.....	106	138	37	1	0	30	37	99	4	6	93	93
New Hampshire.....	55	24	3	5	2	11	44	8	4	0	26	26
New Jersey.....	1,400	1,787	243	231	359	532	738	958	43	64	1,016	1,015
New Mexico.....	252	346	58	67	67	93	117	163	24	23	240	215
New York.....	4,656	6,975	891	1,007	922	1,237	2,681	4,470	119	186	2,453	3,415
North Carolina.....	1,528	2,116	633	496	562	840	306	745	27	35	2,256	1,615
North Dakota.....	49	55	11	16	6	11	19	22	3	2	67	67
Ohio.....	3,132	4,648	671	568	893	1,035	1,447	2,141	121	123	1,572	915
Oklahoma.....	1,078	1,616	186	221	297	468	379	611	41	66	1,279	915
Oregon.....	391	373	97	88	46	29	124	251	122	5	570	315
Pennsylvania.....	1,817	2,463	317	303	544	1,064	618	894	49	107	0	1,315
Rhode Island.....	152	188	45	14	10	18	73	129	7	4	406	115
South Carolina.....	1,719	3,352	406	619	557	1,531	635	1,045	52	92	1,238	1,115
South Dakota.....	69	103	10	20	29	13	26	42	4	7	87	87
Tennessee.....	2,507	3,282	344	498	1,032	1,295	1,039	1,342	79	85	2,011	2,815
Texas.....	2,952	4,084	615	485	991	1,072	1,020	1,512	106	99	1,764	1,715
Utah.....	121	169	31	38	5	17	84	111	1	3	115	115
Vermont.....	36	41	6	11	7	12	20	17	3	1	86	86
Virginia.....	1,466	2,546	419	822	589	911	409	700	36	68	785	2,315
Washington.....	(*)	766	(*)	127	(*)	190	(*)	324	(*)	15	(*)	1,415
West Virginia.....	454	669	103	106	54	98	42	139	9	18	493	315
Wisconsin.....	129	204	45	41	0	0	81	161	3	2	177	215
Wyoming.....	325	132	41	27	99	19	170	69	13	5	30	30
<i>Territories, Possessions and Panama C.Z.</i>												
Alaska.....	20	16	5	8	4	3	3	1	1	1	136	136
Canal Zone.....	165	(*)	21	(*)	30	(*)	97	(*)	6	(*)	82	82
Hawaii.....	170	177	51	38	23	18	84	107	8	13	335	215
Puerto Rico.....	2,349	4,096	352	390	766	755	728	1,024	477	412	1,229	715
Virgin Islands.....	45	46	4	13	29	25	5	7	2	1	19	19
Actual Total† U.S., Territories & Canal Zone....	62,856	90,082	13,021	14,003	17,447	24,118	25,397	38,267	2,691	2,942	54,353	53,515

\*No data available.

†Based on 47 States and the Dist. of Columbia.

\*\*Includes "not stated".

†Based on States reporting in both fiscal periods.

‡Includes all reported cases.

§Included in late and late latent.



# New Cases of Syphilis and Gonorrhea in Cities of 200,000 Population and Over

Health Officers' monthly statement: Reported for the first two months of fiscal years 1944-45 and 1943-44

City	Cases of syphilis and gonorrhea reported for first 2 months of fiscal years below											
	Syphilis										Gonorrhea	
	Total**		Primary and secondary		Early latent		Late and late latent		Congenital		1944-45	1943-44
	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44	1944-45	1943-44		
Total†....	119,231	126,236	23,684	23,025	24,940	26,148	28,141	212,258	2432	2526	113,213	111,416
Akron.....	151	195	42	19	27	56	72	113	10	7	126	90
Atlanta.....	433	675	142	133	119	255	166	278	6	9	572	206
Baltimore....	1,016	2,430	301	202	265	200	313	317	11	11	500	601
Birmingham..	662	966	63	67	170	240	149	257	14	20	113	111
Boston.....	257	303	48	64	80	0	105	189	14	6	283	221
Buffalo.....	(*)	323	(*)	27	(*)	53	(*)	235	(*)	8	(*)	135
Chicago.....	(*)	2,580	(*)	420	(*)	650	(*)	1,440	(*)	70	(*)	2,426
Cincinnati....	390	529	58	67	(§)	(§)	332	462	(§)	(§)	180	194
Cleveland....	761	666	155	107	280	216	310	324	16	19	316	213
Columbus....	257	262	80	43	60	57	112	153	5	9	98	66
Dallas.....	372	431	96	84	115	84	159	260	2	3	169	147
Dayton.....	189	255	25	35	50	75	106	134	8	11	94	61
Denver.....	226	433	60	69	81	102	70	152	5	12	211	294
Detroit.....	1,722	2,141	297	232	609	629	789	1,241	27	39	1,092	977
Honolulu....	46	108	11	21	6	13	27	65	1	9	181	198
Houston.....	293	370	64	58	104	136	113	162	12	14	332	402
Indianapolis..	325	365	66	128	42	1	92	65	4	4	47	15
Jersey City..	74	96	5	13	22	23	41	63	6	7	16	8
Kansas City..	248	299	54	47	59	43	119	193	9	14	180	160
Los Angeles..	1,803	2,134	362	0	399	820	988	1,243	54	71	1,010	816
Louisville....	219	560	56	59	49	88	95	202	12	4	214	156
Memphis.....	1,198	1,184	126	118	594	564	455	491	23	11	921	897
Milwaukee....	70	93	18	9	0	0	51	80	1	1	102	64
Minneapolis..	129	135	36	25	18	27	71	81	4	1	196	157
Newark.....	274	351	64	48	75	86	132	208	3	9	195	150
New Orleans..	361	448	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	460	165
New York....	3,311	4,761	751	769	825	1,079	1,619	2,750	85	117	2,453	2,356
Oakland.....	285	294	36	27	67	75	154	187	7	5	318	215
Oklahoma Cy	258	340	65	49	80	117	72	142	6	6	159	161
Omaha.....	83	91	9	7	15	58	55	21	4	5	77	77
Philadelphia..	953	966	135	53	146	183	143	246	13	8	134	47
Pittsburgh...	(*)	1,454	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)
Portland....	142	172	48	33	22	9	71	130	1	0	278	149
Providence...	66	92	10	7	4	3	38	73	2	1	24	25
Rochester...	40	38	5	8	2	1	33	27	0	2	65	41
St. Louis....	1,057	852	249	122	313	314	464	391	31	25	722	257
St. Paul.....	41	48	9	9	9	15	17	19	2	2	30	67
San Antonio..	179	244	21	23	38	59	114	149	6	13	203	228
San Diego....	274	215	26	12	74	53	141	141	15	9	212	124
San Francisco	463	610	(*)	(*)	(*)	(*)	(*)	(*)	(*)	(*)	387	366
Seattle.....	239	245	57	24	56	45	118	154	1	6	265	288
Syracuse....	94	152	6	5	6	9	80	131	2	7	72	42
Toledo.....	94	202	9	30	15	45	67	122	3	5	35	21
Wash., D. C..	176	1,485	19	199	44	368	88	842	7	24	171	583
Actual Total†	19,231	30,593	3,684	3,472	4,940	6,851	8,141	13,933	432	604	13,213	13,977

\* Data not available.

\*\* Includes "not stated".

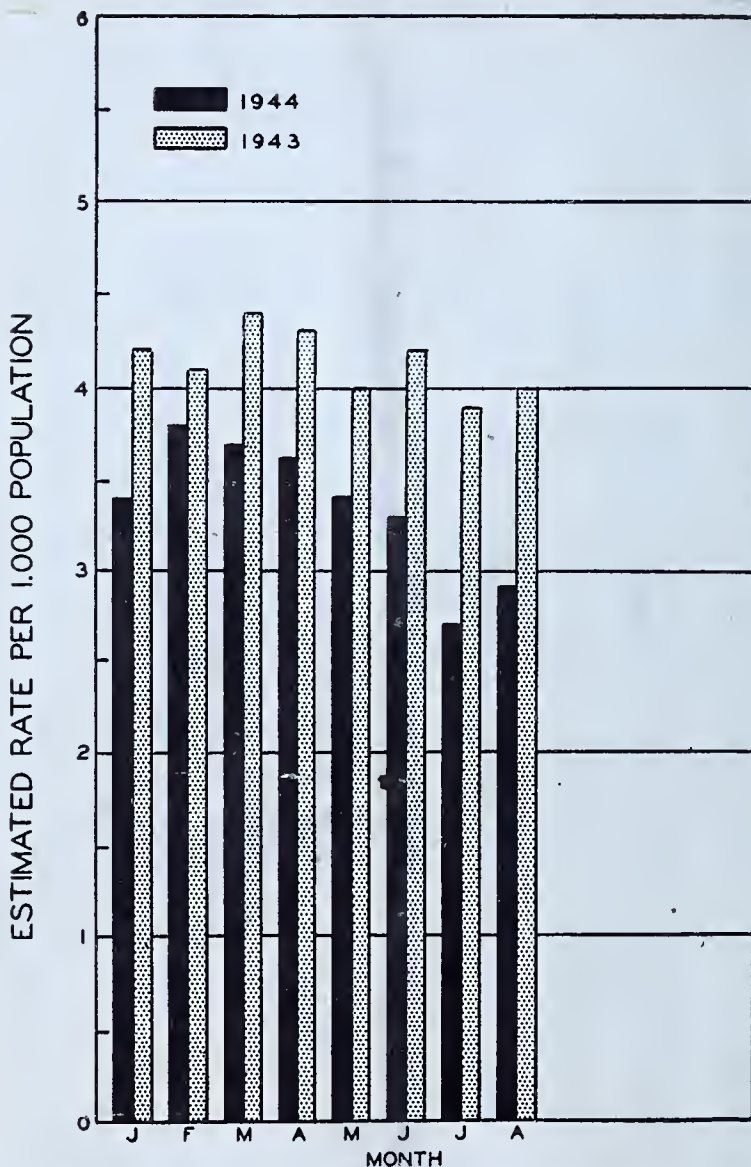
† Based on cities reporting in both fiscal periods.

‡ Includes all reported cases.

§ Included in late and late latent.

<sup>1</sup> Based on 41 cities.

<sup>2</sup> Based on 39 cities.



ANNUAL SYPHILIS CASE RATES  
IN THE UNITED STATES BASED ON PROVISIONAL MONTHLY DATA  
1944 AND 1943



















